consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55736.

In light of an observed sequence homology between the DNA55736 consensus sequence and an EST sequence encompassed within the Merck EST clone no. R88049, the Merck EST clone R88049 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 126 and is herein designated as DNA57693-1424.

Clone DNA57693-1424 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 56-58 and ending at the stop codon at nucleotide positions 416-418 (Figure 126). The predicted polypeptide precursor is 120 amino acids long (Figure 127). The full-length PRO1056 protein shown in Figure 127 has an estimated molecular weight of about 13,345 daltons and a pl of about 5.18. Analysis of the full-length PRO1056 sequence shown in Figure 127 (SEQ ID NO:199) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 18, a transmembrane domain from about amino acid 39 to about amino acid 58, a potential N-glycosylation site from about amino acid 86 to about amino acid 89, protein kinase C phosphorylation sites from about amino acid 36 to about amino acid 38 and from about amino acid 58 to about amino acid 60, a tyrosine kinase phosphorylation site from about amino acid 25 to about amino acid 32 and an amino acid sequence block having homology to channel forming colicin proteins from about amino acid 24 to about amino acid 56. Clone DNA57693-1424 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203008.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 127 (SEQ ID NO:199), evidenced significant homology between the PRO1056 amino acid sequence and the following Dayhoff sequences: PLM_HUMAN, A40533, ATNG_HUMAN, A55571, ATNG_SHEEP, S31524, GEN13025, RIC_MOUSE, A48678 and A10871_1.

EXAMPLE 54: Isolation of cDNA clones Encoding Human PRO826

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 47283. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56000.

In light of an observed sequence homology between the DNA56000 consensus sequence and an EST sequence encompassed within the Merck EST clone no. W69233, the Merck EST clone W69233 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 128 and is herein designated as DNA57694-1341.

Clone DNA57694-1341 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 13-15 and ending at the stop codon at nucleotide positions 310-312 (Figure 128). The predicted polypeptide precursor is 99 amino acids long (Figure 129). The full-length PRO826 protein shown in Figure 129 has an estimated molecular weight of about 11,050 daltons and a pl of about 7.47. Analysis of the full-length PRO826 sequence shown in Figure 129 (SEQ ID NO:201) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 22, potential N-myristoylation sites from about amino acid 22 to about amino acid 27 and from about amino acid 90 to about amino acid 95 and an amino acid sequence block having homology to peroxidase from about amino acid 16 to about amino acid 48. Clone DNA57694-1341 has been deposited with ATCC on June 22, 1998 and is assigned ATCC deposit no. 203017.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 129 (SEQ ID NO:201), evidenced significant homology between the PRO826 amino acid sequence and the following Dayhoff sequences: CCU12315_1, SCU96108_6, CELF39F10_4 and HELT_HELHO.

EXAMPLE 55: Isolation of cDNA clones Encoding Human PRO819

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 49605. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56015.

In light of an observed sequence homology between the DNA56015 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H65785, the Merck EST clone H65785 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 130 and is herein designated as DNA57695-1340.

Clone DNA57695-1340 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 46-48 and ending at the stop codon at nucleotide positions 202-204 (Figure 130). The predicted polypeptide precursor is 52 amino acids long (Figure 131). The full-length PRO819 protein shown in Figure 131 has an estimated molecular weight of about 5,216 daltons and a pl of about 4.67. Analysis of the full-length PRO819 sequence shown in Figure 131 (SEQ ID NO:203) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, a potential N-myristoylation site from about amino acid 2 to about amino acid 7 and a region having homology to immunoglobulin light chain from about amino acid 5 to about amino acid 33. Clone DNA57695-1340 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203006.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 131 (SEQ ID NO:203), evidenced significant homology between the PRO819 amino acid sequence and the following Dayhoff sequences: HSU03899_1, HUMIGLITEB_1, VG28_HSVSA, AF031522_1, PAD1_YEAST and AF045484 1.

EXAMPLE 56: Isolation of cDNA Clones Encoding Human PRO1006

An initial candidate sequence from Incyte cluster sequence no. 45748 was identified using the signal algorithm process described in Example 3 above. This sequence was then aligned with a variety of public and Incyte EST sequences and a consensus sequence designated herein as DNA56036 was derived therefrom.

In light of an observed sequence homology between the DNA56036 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 489737, the Merck EST clone 489737 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 132.

The entire nucleotide sequence of DNA57699-1412 is shown in Figure 132 (SEQ ID NO:204). Clone DNA57699-1412 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 28-30 and ending at the stop codon at nucleotide positions 1204-1206 (Figure 132). The predicted polypeptide precursor is 392 amino acids long (Figure 133). The full-length PRO1006 protein shown in Figure 133 has an estimated molecular weight of about 46,189 daltons and a pl of about 9.04. Clone DNA57699-1412 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:205, the putative signal peptide is at about amino acids 1-23 of SEQ ID NO:205. The N-glycosylation sites are at about amino acids 40-43, 53-56, 204-207 and 373-376 of SEQ ID-NO:205.—An-N-myristoylation-site-is-at-about-amino-acids-273-278 of SEQ-ID-NO:205. The corresponding nucleotides of these amino acid regions and others can be routinely determined given the sequences provided herein.

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EXAMPLE 57: Isolation of cDNA Clones Encoding Human PRO1112

Use of the signal sequence algorithm described in Example 3 above allowed identification of a specific EST cluster sequence. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database 30 (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56018.

In light of an observed sequence homology between the DNA56018 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA223546, the Merck EST clone AA223546 was

purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 134 and is herein designated as DNA57702-1476.

The entire nucleotide sequence of DNA57702-1476 is shown in Figure 134 (SEQ ID NO:206). Clone DNA57702-1476 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 20-22 and ending at the stop codon at nucleotide positions 806-808 of SEQ ID NO:206 (Figure 134).

The predicted polypeptide precursor is 262 amino acids long (Figure 135). The full-length PRO1112 protein shown in Figure 135 has an estimated molecular weight of about 29,379 daltons and a pI of about 8.93. Figure 135 also shows the approximate locations of the signal peptide and transmembrane domains. Clone DNA57702-1476 has been deposited with the ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO1112 polypeptide suggests that it possesses some sequence similarity to other proteins. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some sequence identity between the PRO1112 amino acid sequence and at least the following Dayhoff sequences, MTY20B11_13 (a mycobacterium tuberculosis peptide), F64471, AE000690_6, XLU16364_1, E43259 (H+-transporting ATP synthase) and PIGSLADRXE_1 (MHC class II histocompatibility antigen).

EXAMPLE 58: Isolation of cDNA clones Encoding Human PRO1074

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence (Incyte cluster sequence No. 42586). This cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ[™], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56251.

In light of an observed sequence homology between the DNA56251 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA081912, the Merck EST clone AA081912 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 136 and is the full-length DNA sequence for PRO1074. Clone DNA57704-1452 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209953.

The entire nucleotide sequence of DNA57704-1452 is shown in Figure 136 (SEQ ID NO:208). Clone DNA57704-1452 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 322-324 and ending at the stop codon at nucleotide positions 1315-1317 (Figure 136). The predicted polypeptide precursor is 331 amino acids long (Figure 137). The full-length PRO1074 protein shown in Figure 137 has an estimated molecular weight of about 39,512 Daltons and a pl of about 8.03. Analysis of the full-

length PRO1074 sequence shown in Figure 137 (SEQ ID NO:209) evidences the presence of the following features: a transmembrane domain at about amino acids 20 to 39; potential N-glycosylation sites at about amino acids 72 to 75, 154 to 157, 198 to 201, 212 to 215, and 326 to 329; a glycosaminoglycan attachment site at about amino acids 239 to 242, and a Ly-6/u-PAR domain at about amino acids 23 to 36.

Analysis of the amino acid sequence of the full-length PRO1074 polypeptide suggests that it possesses significant sequence similarity to beta 1,3-galactosyltransferase, thereby indicating that PRO1074 may be a novel member of the galactosyltransferase family of proteins. Analysis of the amino acid sequence of the full-length PRO1074 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1074 amino acid sequence and the following Dayhoff sequences: AF029792_1, P_R57433, DMU41449_1, AC000348_14, P_R47479, CET09F5_2, CEF14B6_4, CET15D6_5, CEC54C8_4, and CEE03H4_10.

Clone DNA57704-1452 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209953.

EXAMPLE 59: Isolation of cDNA clones Encoding Human PRO1005

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, Incyte cluster sequence no. 49243. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56380.

In light of an observed sequence homology between the DNA56380 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA256657, the Merck EST clone AA256657 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 138 and is herein designated as DNA57708-1411.

The full length clone shown in Figure 138 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 30-32 and ending at the stop codon found at nucleotide positions 585-587 (Figure 138; SEQ ID NO:210). The predicted polypeptide precursor (Figure 139, SEQ ID NO:211) is 185 amino acids long. PRO1005 has a calculated molecular weight of approximately 20,331 daltons and an estimated pI of approximately 5.85. Clone DNA57708-1411 was deposited with the ATCC June 23, 1998, and is assigned ATCC deposit no. 203021.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 139 (SEQ ID NO:211), evidenced some homology between the PRO1005 amino acid sequence and the following Dayhoff sequences: DDU07187_1, DDU87912_1, CELD1007_14, A42239, DDU42597_1, CYAG_DICDI, S50452, MRKC_KLEPN, P-R41998,

and XYNA_RUMFL.

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EXAMPLE 60: Isolation of cDNA clones Encoding Human PRO1073

An initial DNA sequence referred to herein as DNA55938 and shown in Figure 142 (SEQ ID NO:214) was identified using a yeast screen, in a human SK-Lu-1 adenocarcinoma cell line cDNA library that preferentially represents the 5' ends of the primary cDNA clones. DNA55938 was then compared to ESTs from public databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA), using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. The ESTs were clustered and assembled into a consensus DNA sequence using the computer program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained is designated herein as DNA56411.

In light of an observed sequence homology between the DNA56411 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H86027, the Merck EST clone H86027 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 140.

The full length DNA57710-1451 clone shown in Figure 140 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 345-347 and ending at the stop codon found at nucleotide positions 1242-1244 (Figure 140; SEQ ID NO:212). The predicted polypeptide precursor (Figure 141, SEQ ID NO:213) is 299 amino acids long. PRO1073 has a calculated molecular weight of approximately 34,689 daltons and an estimated pI of approximately 11.49. The PRO1073 polypeptide has the following additional features: a signal peptide at about amino acids 1-31, sequence identity to bZIP transcription factor basic domain signature at about amino acids, a potential N-glycosylation site at about amino acids 2-5, and sequence identity with protamine P1 proteins at about amino acids 158-183.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 141 (SEQ ID NO:213), revealed some sequence identity between the PRO1073 amino acid sequence and the following Dayhoff sequences: MMU37351_1, ATAC00250510T9J22.10, S59043, ENXNUPR_1, B47328, SR55_DROME, S26650, SON_HUMAN, VIT2_CHICK, and XLC4SRPRT_1.

Clone DNA57710-1451 was deposited with the ATCC on July 1, 1998 and is assigned ATCC deposit no. 203048.

EXAMPLE 61: Isolation of cDNA clones Encoding Human PRO1152

A cDNA clone (DNA57711-1501) encoding a native human PRO1152 polypeptide was identified by employing a yeast screen, in a human infant brain cDNA library that preferentially represents the 5' ends of the primary cDNA clones. Specifically, a yeast screen was employed to identify a cDNA designated herein as DNA55807 (SEQ ID NO:217; see Figure 145).

In light of an observed sequence homology between the DNA55807 sequence and an EST sequence encompassed within the Merck EST clone no. R56756, the Merck EST clone R56756 was purchased and the

cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 143.

The full-length DNA57711-1501 clone shown in Figure 143 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon at nucleotide positions 1495-1497 (Figure 143). The predicted polypeptide precursor is 479 amino acids long (Figure 144). The full-length PRO1152 protein shown in Figure 144 has an estimated molecular weight of about 53,602 daltons and a pl of about 8.82. Analysis of the full-length PRO1152 sequence shown in Figure 144 (SEQ ID NO:216) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, transmembrane domains from about amino acid 133 to about amino acid 155, from about amino acid 168 to about amino acid 187, from about amino acid 229 to about amino acid 247, from about amino acid 264 to about amino acid 390 and from about amino acid 309 to about amino acid 330, from about amino acid 371 to about amino acid 390 and from about amino acid 441 to about amino acid 464, potential N-glycosylation sites from about amino acid 34 to about amino acid 37 and from about amino acid 387 to about amino acid 390 and an amino acid sequence block having homology to a respiratory-chain NADH dehydrogenase subunit from about amino acid 243 to about amino acid 287. Clone DNA57711-1501 has been deposited with ATCC on July 1, 1998 and is assigned ATCC deposit no. 203047.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 144 (SEQ ID NO:216), evidenced significant homology between the PRO1152 amino acid sequence and the following Dayhoff sequences: AF052239_1, SYNN9CGA_1, SFCYTB2_1, GEN12507, P_R11769, MTV025_109, C61168, S43171, P_P61689 and P_P61696.

EXAMPLE 62: Isolation of cDNA clones Encoding Human PRO1136

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 109142. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56039.

In light of an observed sequence homology between the DNA56039 consensus sequence and an EST sequence encompassed within the Merck EST clone no. HSC1NF011, the Merck EST clone HSC1NF011 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 146 and is herein designated as DNA57827-1493.

Clone DNA57827-1493) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 216-218 and ending at the stop codon at nucleotide positions 2112-2114 (Figure 146).

The predicted polypeptide precursor is 632 amino acids long (Figure 147). The full-length PRO1136 protein shown in Figure 147 has an estimated molecular weight of about 69,643 daltons and a pl of about 8.5. Analysis of the full-length PRO1136 sequence shown in Figure 147 (SEQ ID NO:219) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15 and potential N-glycosylation sites from about amino acid 108 to about amino acid 11, from about amino acid 157 to about amino acid 160, from about amino acid 289 to about amino acid 292 and from about amino acid 384 to about amino acid 387. Clone DNA57827-1493 has been deposited with ATCC on July 1, 1998 and is assigned ATCC deposit no. 203045.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 147 (SEQ ID NO:219), evidenced significant homology between the PRO1136 amino acid sequence and the following Dayhoff sequences: AF034746_1, AF034745_1, MMAF000168_19, HSMUPP1_1; AF060539_1, SP97_RAT, I38757, MMU93309_1, CEK01A6_4 and HSA224747_1.

EXAMPLE 63: Isolation of cDNA clones Encoding Human PRO813

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence no. 45501. The Incyte EST cluster sequence no. 45501 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56400.

In light of an observed sequence homology between the DNA56400 consensus sequence and an EST sequence encompassed within the Merck EST clone no. T90592, the Merck EST clone T90592 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 148 and is herein designated DNA57834-1339.

The full length clone shown in Figure 148 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 109-111 and ending at the stop codon found at nucleotide positions 637-639 (Figure 149; SEQ ID NO:221). The predicted polypeptide precursor is 176 amino acids long, has a calculated molecular weight of approximately 19,616 daltons and an estimated pl of approximately 7.11. Analysis of the full-length PRO813 sequence shown in Figure 149 (SEQ ID NO:221) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 26 and potential N-myristoylation sites from about amino acid 48 to about amino acid 53, from about amino acid 153 to about amino acid 158, from about amino acid 156 to about amino acid 161 and from about amino acid 167 to about amino acid 172. Clone DNA57834-1339 has been deposited with the ATCC on June 9, 1998 and is assigned ATCC deposit no. 209954.

Analysis of the amino acid sequence of the full-length PRO813 polypeptide suggests that it possesses sequence similarity to the pulmonary surfactant-associated protein C. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO813 amino acid sequence and the following Dayhoff sequences, PSPC_MUSVI, P_P92071, G02964, P_R65489, P_P82977, P_R84555, S55542, MUSIGHAJ_1 and PH1158.

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EXAMPLE 64: Isolation of cDNA Clones Encoding Human PRO809

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence. The Incyte EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQTM, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56418.

In light of an observed sequence homology between the DNA56418 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H74302, the Merck EST clone H74302 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 150 and is herein designated DNA57836-1338.

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The entire nucleotide sequence of DNA57836-1338 is shown in Figure 150 (SEQ ID NO:222). Clone DNA57836-1338 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 63-65 and ending at the stop codon at nucleotide positions 858-860 of SEQ ID NO:222 (Figure 150). The predicted polypeptide precursor is 265 amino acids long (Figure 151). The full-length PRO809 protein shown in Figure 151 has an estimated molecular weight of about 29,061 daltons and a pl of about 9.18. Figure 151 further shows the approximate positions of the signal peptide and N-glysosylation sites. The corresponding nucleotides can be determined by referencing Figure 150. Clone DNA57836-1338 has been deposited with ATCC on June 23, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

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Analysis of the amino acid sequence of the full-length PRO809 polypeptide suggests that it possesses some sequence similarity to the heparin sulfate proteoglycan and to endothelial cell adhesion molecule-1. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO809 amino acid sequence and the following Dayhoff sequences, PGBM_MOUSE, D82082_1 and PW14158.

35 EXAMPLE 65: Isolation of cDNA Clones Encoding Human PRO791

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence. The Incyte EST cluster sequence was then compared to a variety of expressed

sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQTM, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56429.

In light of an observed sequence homology between the DNA56429 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 36367, the Merck EST clone 36367 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 152 and is herein designated DNA57838-1337.

The entire nucleotide sequence of DNA57838-1337 is shown in Figure 152 (SEQ ID NO:224). Clone DNA57838-1337 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 9-11 and ending at the stop codon at nucleotide positions 747-749 of SEQ ID NO:224 (Figure 152). The predicted polypeptide precursor is 246 amino acids long (Figure 153). The full-length PRO791 protein shown in Figure 153 has an estimated molecular weight of about 27,368 daltons and a pI of about 7.45. Figure 153 also shows the approximate locations of the signal peptide, the transmembrane domain, N-glycosylation sites and a region conserved in extracellular proteins. The corresponding nucleotides of one embodiment provided herein can be identified by referencing Figure 152. Clone DNA57838-1337 has been deposited with ATCC on June 23, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO791 polypeptide suggests that it has sequence similarity with MHC-I antigens, thereby indicating that PRO791 may be related to MHC-I antigens. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some sequenc identity between the PRO791 amino acid sequence and the following Dayhoff sequences, AF034346_1, MMQ1K5_1 and HFE HUMAN.

EXAMPLE 66: Isolation of cDNA clones Encoding Human PRO1004

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence, Incyte cluster sequence No. 73681. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated as DNA56516.

In light of an observed sequence homology between the DNA56516 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H43837, the Merck EST clone H43837 was purchased

and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 154.

The full length clone shown in Figure 154 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 119-121 and ending at the stop codon at nucleotide positions 464-466 (Figure 154; SEQ ID NO:226). The predicted polypeptide precursor is 115 amino acids long (Figure 155; SEQ ID NO:227). The full-length PRO1004 protein shown in Figure 155 has an estimated molecular weight of about 13,649 daltons and a pI of about 9.58. Analysis of the full-length PRO1004 sequence shown in Figure 155 (SEQ ID NO:227) evidences the presence of the following features: a signal peptide at about amino acids 1-24, a microbodies C-terminal targeting signal at about amino acids 113-115, a potential N-glycosylation site at about amino acids 71-74, and a domain having sequence identity with dihydrofolate reductase proteins at about amino acids 22-48.

Analysis of the amino acid sequence of the full-length PRO1004 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1004 amino acid sequence and the following Dayhoff sequences: CELR02D3_7, LECI_MOUSE, AF006691_3, SSZ97390_1, SSZ97395_1, and SSZ97400_1.

Clone DNA57844-1410 was deposited with the ATCC on June 23, 1998, and is assigned ATCC deposit no. 203010.

EXAMPLE 67: Isolation of cDNA clones Encoding Human PRO1111

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An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which had homology to insulin-like growth factor binding protein.

RNA for construction of cDNA libraries was isolated from human fetal brain. The cDNA libraries used to isolate the cDNA clones encoding human PRO1111 were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI.

The human fetal brain cDNA libraries (prepared as described above), were screened by hybridization with a synthetic oligonucleotide probe based upon the Incyte EST sequence described above:

30 5'-CCACCACCTGGAGGTCCTGCAGTTGGGCAGGAACTCCATCCGGCAGATTG-3' (SEQ ID NO:251).

An identified cDNA clone was sequenced in entirety. The entire nucleotide sequence of PRO1111 is shown in Figure 156 (SEQ ID NO:228). Clone DNA58721-1475 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 57-59 and a stop codon at nucleotide positions 2016-2018 (Figure 156; SEQ ID NO:228). The predicted polypeptide precursor is 653 amino acids long (Figure 157). The transmembrane domains are at positions 21-40 (type II) and 528-548. Clone DNA58721-1475 has been deposited with ATCC and is assigned ATCC deposit no. 203110. The full-length PRO1111 protein shown in Figure 157 has an estimated molecular weight of about 72,717 daltons and a pI of about 6.99.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 157 (SEQ ID NO:229), revealed some sequence identity between the PRO1111 amino acid sequence and the following Dayhoff sequences: A58532, D86983_1, RNPLGPV_1, PGS2_HUMAN, AF038127_1, ALS_MOUSE, GPV_HUMAN, PGS2_BOVIN, ALS_PAPPA and I47020.

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EXAMPLE 68: Isolation of cDNA clones Encoding Human PRO1344

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA33790. Based on the DNA33790 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1344.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-AGGTTCGTGATGGAGACAACCGCG-3' (SEQ ID NO:232)

reverse PCR primer 5'-TGTCAAGGACGCACTGCCGTCATG-3' (SEQ ID NO:233)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA33790 sequence which had the following nucleotide sequence

hybridization probe

5'-TGGCCAGATCATCAAGCGTGTCTGTGGCAACGAGCGGCCAGCTCCTATCC-3' (SEQ ID NO:234)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1344 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1344 (designated herein as DNA58723-1588 [Figure 158, SEQ ID NO:230]); and the derived protein sequence for PRO1344.

The entire nucleotide sequence of DNA58723-1588 is shown in Figure 158 (SEQ ID NO:230). Clone DNA58723-1588 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 26-28 and ending at the stop codon at nucleotide positions 2186-2188 (Figure 158). The predicted polypeptide precursor is 720 amino acids long (Figure 159). The full-length PRO1344 protein shown in Figure 159 has an estimated molecular weight of about 80,199 daltons and a pl of about 7.77. Analysis of the full-length PRO1344 sequence shown in Figure 159 (SEQ ID NO:231) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 23, an EGF-like domain cysteine protein signature sequence from about amino acid 260 to about amino acid 271, potential N-glycosylation sites from about amino acid 96 to about amino acid 99, from about amino acid 279 to about amino acid 282, from about amino acid 316 to about amino acid 319, from about amino acid 451 to about amino acid 454 and from about amino acid 614 to about amino acid 617, an amino acid sequence block having homology to serine proteases, trypsin family from about amino acid 489 to about amino acid 505 and a CUB domain protein profile sequence from about amino

acid 150 to about amino acid 166. Clone DNA58723-1588 has been deposited with ATCC on August 18, 1998 and is assigned ATCC deposit no. 203133.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 159 (SEQ ID NO:231), evidenced significant homology between the PRO1344 amino acid sequence and the following Dayhoff sequences: S77063_1, CRAR_MOUSE, P_R74775, P_P90070, P_R09217, P_P70475, HSBMP16_1 and U50330_1.

EXAMPLE 69: Isolation of cDNA clones Encoding Human PRO1109

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA52642. The consensus DNA sequence was obtained by extending using repeated cycles of BLAST and phrap a previously obtained consensus sequence as far as possible using the sources of EST sequences discussed above. Based on the DNA52642 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1109.

PCR primers (forward and reverse) were synthesized:

15 <u>forward PCR primer</u> 5'-CCTTACCTCAGAGGCCAGAGCAAGC-3' (SEQ ID NO:237) <u>reverse PCR primer</u> 5'-GAGCTTCATCCGTTCTGCGTTCACC-3' (SEQ ID NO:238)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA52642 sequence which had the following nucleotide sequence

hybridization probe

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20 5'-CAGGAATGTAAAGCTTTACAGAGGGTCGCCATCCTCGTTCCCCACC-3' (SEQ ID NO:239)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1109 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human SK-Lu-1 adenocarcinoma cell tissue (LIB247).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1109 (designated herein as DNA58737-1473 [Figure 160, SEQ ID NO:235]) and the derived protein sequence for PRO1109.

The entire nucleotide sequence of DNA58737-1473 is shown in Figure 160 (SEQ ID NO:235). Clone DNA58737-1473 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 119-120 and ending at the stop codon at nucleotide positions 1151-1153 (Figure 160). The predicted polypeptide precursor is 344 amino acids long (Figure 161). The full-length PRO1109 protein shown in Figure 161 has an estimated molecular weight of about 40,041 daltons and a pI of about 9.34. Analysis of the full-length PRO1109 sequence shown in Figure 161 (SEQ ID NO:236) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 27, potential N-glycosylation sites from about amino acid 4 to about amino acid 7, from about amino acid 220 to about amino acid 223 and from about amino acid 338 and an amino acid sequence block having homology to xylose isomerase proteins from about amino acid 191 to about amino acid 201. Clone DNA58737-1473 has been deposited with ATCC

on August 18, 1998 and is assigned ATCC deposit no. 203136.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 161 (SEQ ID NO:236), evidenced significant homology between the PRO1109 amino acid sequence and the following Dayhoff sequences: HSUDPGAL_1, HSUDPB14_1, NALS_BOVIN, HSU10473_1, CEW02B12_11, YNJ4_CAEEL, AE000738_11, CET24D1_1, S48121 and CEGLY9_1.

EXAMPLE 70: Isolation of cDNA clones Encoding Human PRO1383

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA53961. Based on the DNA53961 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1383.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CATTTCCTTACCCTGGACCCAGCTCC-3' (SEQ ID NO:242)

15 reverse PCR primer 5'-GAAAGGCCCACAGCACATCTGGCAG-3' (SEQ ID NO:243)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA53961 sequence which had the following nucleotide sequence

hybridization probe

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5'-CCACGACCCGAGCAACTTCCTCAAGACCGACTTGTTTCTCTACAGC-3' (SEQ ID NO:244)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1383 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal brain tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1383 (designated herein as DNA58743-1609 [Figure 162, SEQ ID NO: 240]) and the derived protein sequence for PRO1383.

The entire nucleotide sequence of DNA58743-1609 is shown in Figure 162 (SEQ ID NO:240). Clone DNA58743-1609 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 122-124 and ending at the stop codon at nucleotide positions 1391-1393 (Figure 162). The predicted polypeptide precursor is 423 amino acids long (Figure 163). The full-length PRO1383 protein shown in Figure 163 has an estimated molecular weight of about 46,989 daltons and a pl of about 6.77. Analysis of the full-length PRO1383 sequence shown in Figure 163 (SEQ ID NO:241) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, a transmembrane domain from about amino acid 369 to about amino acid 361, from about amino acid 34 to about amino acid 37, from about amino acid 58 to about amino acid 61, from about amino acid 142 to about amino acid 145, from about amino acid 197 to about amino acid 200, from about amino acid 300 to about amino acid 303 and from about amino acid 364 to about amino acid 367. Clone DNA58743-1609 has been deposited with ATCC on

August 25, 1998 and is assigned ATCC deposit no. 203154.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 163 (SEQ ID NO:241), evidenced significant homology between the PRO1383 amino acid sequence and the following Dayhoff sequences: NMB_HUMAN, QNR_COTJA, P_W38335, P115_CHICK, P_W38164, A45993_1, MMU70209_1, D83704_1 and P_W39176.

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EXAMPLE 71: Isolation of cDNA Clones Encoding Human PRO1003

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence designated herein as 43055. This sequence was then compared to a variety of EST databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated consen01.

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2849382, the Incyte EST clone 2849382 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 164.

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The entire nucleotide sequence of DNA58846-1409 is shown in Figure 164 (SEQ ID NO:245). Clone DNA58846-1409 contains a single open reading frame with an apparent translational initiation site at nucleotide positions-41-43-and-ending-at-the-stop-codon-at-nucleotide positions-293-295 (Figure 164). The predicted polypeptide precursor is 84 amino acids long (Figure 165). The full-length PRO1003 protein shown in Figure 165 has an estimated molecular weight of about 9,408 daltons and a pI of about 9.28. Analysis of the full-length PRO1003 sequence shown in Figure 165 (SEQ ID NO:246) evidences the presence of a signal peptide at amino acids 1 to about 24, and a cAMP- and cGMP-dependent protein kinase phosphorylation site at about amino acids 58 to about 61. Analysis of the amino acid sequence of the full-length PRO1003 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1003 amino acid sequence and the following Dayhoff sequences: AOPCZA363_3, SRTX_ATREN, A48298, MHVJHMS_1, VGL2_CVMJH, 30 DHDHTC2_2, CORT_RAT, TAL6_HUMAN, P_W14123, and DVUFI 2.

EXAMPLE 72: Isolation of cDNA Clones Encoding Human PRO1108

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA53237.

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In light of an observed sequence homology between the DNA53237 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2379881, the Incyte EST clone 2379881 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

PCT/US99/12252 WO 99/63088

The sequence of this cDNA insert is shown in Figure 166 and is herein designated DNA58848-1472.

The entire nucleotide sequence of DNA58848-1472 is shown in Figure 166 (SEQ ID NO:247). Clone DNA58848-1472 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 77-79 and ending at the stop codon at nucleotide positions 1445-1447 (Figure 166). The predicted polypeptide precursor is 456 amino acids long (Figure 167). The full-length PRO1108 protein shown in Figure 5 167 has an estimated molecular weight of about 52,071 daltons and a pI of about 9.46. Analysis of the fulllength PRO1108 sequence shown in Figure 167 (SEQ ID NO:248) evidences the presence of the following:type Il transmembrane domains from about amino acid 22 to about amino acid 42, from about amino acid 156 to about amino acid 176, from about amino acid 180 to about amino acid 199 and from about amino acid 369 to about amino acid 388, potential N-glycosylaion sites from about amino acid 247 to about amino acid 250, from about amino acid 327 to about amino acid 330, from about amino acid 328 to about amino acid 331 and from about amino acid 362 to about amino acid 365 and an amino acid block having homology to ER lumen protein retaining receptor protein from about amino acid 153 to about amino acid 190. Clone DNA58848-1472 has been deposited with ATCC on June 9, 1998 and is assigned ATCC deposit no. 209955.

Analysis of the amino acid sequence of the full-length PRO1108 polypeptide suggests that it possesses significant sequence similarity to the LPAAT protein, thereby indicating that PRO1108 may be a novel LPAAT homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO1108 amino acid sequence and the following Dayhoff sequences, AF015811_1, CER07E3_2, YL35_CAEEL, S73863, CEF59F4_4, P_W06422, MMU41736_1, MTV008_39, P_R99248 and Y67_BPT7.

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EXAMPLE 73: Isolation of cDNA Clones Encoding Human PRO1137

The extracellular domain (ECD) sequences (including the secretion signal, if any) of from about 950 known secreted proteins from the Swiss-Prot public protein database were used to search expressed sequence tag (EST) databases. The EST databases included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequence. Using this procedure, Incyte EST No. 3459449, also referred to herein as "DNA7108", was identified as an EST having a BLAST score of 70 or greater that did not encode a known protein.

A consensus DNA sequence was assembled relative to the DNA7108 sequence and other ESTs using repeated cycles of BLAST and the program "phrap" (Phil Green, Univ. of Washington, Seattle, WA). The consensus sequence obtained therefrom is referred to herein as DNA53952.

In light of an observed sequence homology between the DNA53952 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3663102, the Incyte EST clone 3663102 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 168.

The entire nucleotide sequence of DNA58849-1494 is shown in Figure 168 (SEQ ID NO:249). Clone DNA58849-1494 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 77-79 and ending at the stop codon at nucleotide positions 797-799 (Figure 168). The predicted polypeptide precursor is 240 amino acids long (Figure 169). The full-length PRO1137 protein shown in Figure 169 has an estimated molecular weight of about 26,064 daltons and a pI of about 8.65. Analysis of the full-length PRO1137 sequence shown in Figure 169 (SEQ ID NO:250) evidences the presence of a signal peptide at about amino acids 1 to 14 and a potential N-glycosylation site at about amino acids 101-105.

Analysis of the amino acid sequence of the full-length PRO1137 polypeptide suggests that it possesses significant sequence similarity to ribosyltransferase thereby indicating that PRO1137 may be a novel member of the ribosyltransferase family of proteins. Analysis of the amino acid sequence of the full-length PRO1137 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1137 amino acid sequence and the following Dayhoff sequences: MMART5_1, NARG_MOUSE, GEN11909, GEN13794, GEN14406, MMRNART62_1, and P_R41876.

EXAMPLE 74: Isolation of cDNA clones Encoding Human PRO1138

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence, Incyte cluster sequence no. 165212. This cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQTM, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA-sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated as DNA54224. The assembly included a proprietary Genentech EST designated herein as DNA49140 (Figure 172; SEQ ID NO:254).

In light of an observed sequence homology between the DNA54224 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3836613, the Incyte EST clone 3836613 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 170 and is the full-length DNA sequence for PRO1138. Clone DNA58850-1495 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209956.

The entire nucleotide sequence of DNA58850-1495 is shown in Figure 170 (SEQ ID NO:252). Clone DNA58850-1495 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 38-40 and ending at the stop codon at nucleotide positions 1043-1045 (Figure 170). The predicted polypeptide precursor is 335 amino acids long (Figure 171). The full-length PRO1138 protein shown in Figure 171 has an estimated molecular weight of about 37,421 Daltons and a pl of about 6.36. Analysis of the full-length PRO1138 sequence shown in Figure 171 (SEQ ID NO:253) evidences the presence of the following features: a signal peptide at about amino acid 1 to about amino acid 22; a transmembrane domain at about amino

PCT/US99/12252 WO 99/63088

acids 224 to about 250; a leucine zipper pattern at about amino acids 229 to about 250; and potential Nglycosylation sites at about amino acids 98-101, 142-145, 148-151, 172-175, 176-179, 204-207, and 291-295.

Analysis of the amino acid sequence of the full-length PRO1138 polypeptide suggests that it possesses significant sequence similarity to the CD84, thereby indicating that PRO1138 may be a novel member of the Ig superfamily of polypeptides. More particularly, analysis of the amino acid sequence of the full-length PRO1138 5 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1138 amino acid sequence and the following Dayhoff sequences: HSU82988_1, HUMLY9_1, P_R97631, P_R97628, P_R97629, P_R97630, CD48_RAT, CD2_HUMAN, P_P93996, and HUMBGP_1.

Clone DNA58850-1495 was deposited with ATCC on June 9, 1998, and is assigned ATCC deposit no. 209956.

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EXAMPLE 75: Isolation of cDNA clones Encoding Human PRO1054

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 66212. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) 15 and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55722.

In light of an observed sequence homology between the DNA55722 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 319751, the Incyte EST clone 319751 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 173 and is herein designated as DNA58853-1423.

Clone DNA58853-1423 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 46-48 and ending at the stop codon at nucleotide positions 586-588 (Figure 173). The predicted polypeptide precursor is 180 amino acids long (Figure 174). The full-length PRO1054 protein shown in Figure 174 has an estimated molecular weight of about 20,638 daltons and a pl of about 5.0. Analysis of the full-length PRO1054 sequence shown in Figure 174 (SEQ ID NO:256) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 18, a leucine zipper pattern from about amino acid 155 to about amino acid 176 and amino acid sequence blocks having homology to lipocalin proteins from about amino acid 27 to about amino acid 38 and from about amino acid 110 to about amino acid 120. Clone DNA58853-1423 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203016.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 174 (SEQ ID NO:256), evidenced significant homology between the PRO1054 amino acid sequence and the following Dayhoff sequences: MUP1_MOUSE, MUP6_MOUSE, MUP2_MOUSE, MUP8_MOUSE, MUP5_MOUSE, MUP4_MOUSE, S10124,

MUPM MOUSE, MUP_RAT and ECU70823_1.

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EXAMPLE 76: Isolation of cDNA clones Encoding Human PRO994

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 157555. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55728.

In light of an observed sequence homology between the DNA55728 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2860366, the Incyte EST clone 2860366 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 175 and is herein designated as DNA58855-1422.

Clone DNA58855-1422 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 31-33 and ending at the stop codon at nucleotide positions 718-720 (Figure 175). The predicted polypeptide precursor is 229 amino acids long (Figure 176). The full-length PRO994 protein shown in Figure 176 has an estimated molecular weight of about 25,109 daltons and a pI of about 6.83. Analysis of the full-length PRO994 sequence shown in Figure 176 (SEQ ID NO:258) evidences the presence of the following: transmembrane domains from about amino acid 10 to about amino acid 31, from about amino acid 50 to about amino acid 72, from about amino acid 87 to about amino acid 110 and from about amino acid 191 to about amino acid 213, potential N-glycosylation sites from about amino acid 80 to about amino acid 83, from about amino acid 132 to about amino acid 135, from about amino acid 148 to about amino acid 151 and from about amino acid 163 to about amino acid 166 and an amino acid block having homology to TNFR/NGFR cysteine-rich region proteins from about amino acid 4 to about amino acid 11. Clone DNA58855-1422 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203018.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 176 (SEQ ID NO:258), evidenced significant homology between the PRO994 amino acid sequence and the following Dayhoff sequences: AF027204_1, TAL6_HUMAN, ILT4_HUMAN, JC6205, MMU57570_1, S40363, ETU56093_1, S42858, P_R66849 and P R74751.

EXAMPLE 77: Isolation of cDNA clones Encoding Human PRO812

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 170079. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank)

and a proprietary EST DNA database (Lifeseq[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated as DNA55721.

In light of an observed sequence homology between the DNA55721 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 388964, the Incyte EST clone 388964 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 177 and is herein designated as DNA59205-1421.

Clone DNA59205-1421 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 55-57 and ending at the stop codon at nucleotide positions 304-306 (Figure 177). The predicted polypeptide precursor is 83 amino acids long (Figure 178). The full-length PRO812 protein shown in Figure 178 has an estimated molecular weight of about 9,201 daltons and a pl of about 9.3. Analysis of the full-length PRO812 sequence shown in Figure 178 (SEQ ID NO:260) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15, a cAMP- and cGMP-dependent protein kinase phosphorylation site from about amino acid 73 to about amino acid 76 and protein kinase C phosphorylation sites from about amino acid 70 to about amino acid 72 and from about amino acid 76 to about amino acid 78. Clone DNA59205-1421 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203009.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 178 (SEQ ID NO:260), evidenced significant homology between the PRO812 amino acid sequence and the following Dayhoff sequences: P_W35802, P_W35803, PSC1_RAT, S68231, GEN13917, PSC2_RAT, CC10_HUMAN, UTER_RABIT, AF008595_1 and A56413.

25 EXAMPLE 78: Isolation of cDNA clones Encoding Human PRO1069

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence designated herein as 100727. This sequence was then compared to a proprietary EST DNA database (LIFESEQTM, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56001.

In light of an observed sequence homology between the DNA56001 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3533881, the Incyte EST clone 3533881 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 179 and is the full-length DNA sequence for PRO1069.

Clone DNA59211-1450 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209960.

The entire nucleotide sequence of DNA59211-1450 is shown in Figure 179 (SEQ ID NO:261). Clone DNA59211-1450 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 197-199 and ending at the stop codon at nucleotide positions 464-466. The predicted polypeptide precursor is 89 amino acids long (Figure 180). The full-length PRO1069 protein shown in Figure 180 has an estimated molecular weight of about 9,433 daltons and a pI of about 8.21. Analysis of the full-length PRO1069 sequence shown in Figure 180 (SEQ ID NO:262) evidences the presence of the following features: a signal peptide sequence at amino acid 1 to about 16; a transmembrane domain at about amino acids 36 to about 59; potential N-myristoylation sites at about amino acids 41-46, 45-50, and 84-89; and homology with extracellular proteins SCP/Tpx-1/Ag5/PR-1/Sc7 at about amino acids 54 to about 66.

Analysis of the amino acid sequence of the full-length PRO1069 polypeptide suggests that it possesses significant sequence similarity to CHIF, thereby indicating that PRO1069 may be a member of the CHIF family of polypeptides. More particularly, analysis of the amino acid sequence of the full-length PRO1069 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1069 amino acid sequence and the following Dayhoff sequences: CHIF_RAT, A55571, PLM_HUMAN, A40533, ATNG_BOVIN, RIC_MOUSE, PETD_SYNY3, VTB1_XENLA, A05009, and S75086.

Clone DNA59211-1450 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209960.

20 EXAMPLE 79: Isolation of cDNA Clones Encoding Human PRO1129

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence designated herein as 98833.—The Incyte EST cluster sequence no. 98833 sequence—was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQTM, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56038.

In light of an observed sequence homology between the DNA56038 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1335241, the Incyte EST clone 1335241 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 181 and is herein designated DNA59213-1487.

The full length clone shown in Figure 181 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 42-44 and ending at the stop codon found at nucleotide positions 1614-1616 (Figure 181; SEQ ID NO:263). The predicted polypeptide precursor is 524 amino acids long, has a calculated molecular weight of approximately 60,310 daltons and an estimated pl of approximately 7.46.

Analysis of the full-length PRO1129 sequence shown in Figure 182 (SEQ ID NO:264) evidences the presence of the following: type II transmembrane domains from about amino acid 13 to about amino acid 32 and from about amino acid 77 to about amino acid 102, a cytochrome P-450 cysteine heme-iron ligand signature sequence from about amino acid 461 to about amino acid 470 and potential N-glycosylation sites from about amino acid 112 to about amino acid 115 and from about amino acid 168 to about amino acid 171. Clone DNA59213-1487 has been deposited with the ATCC on June 9, 1998 and is assigned ATCC deposit no. 209959.

Analysis of the amino acid sequence of the full-length PRO1129 polypeptide suggests that it possesses sequence similarity to the cytochrome P-450 family of proteins. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO1129 amino acid sequence and the following Dayhoff sequences, AC004523_1, S45702, AF054821_1 and 153015.

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EXAMPLE 80: Isolation of cDNA clones Encoding Human PRO1068

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated Incyte cluster no. 141736. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs was derived from a human mast cell line from a patient with mast cell leukemia. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56094.

In light of an observed sequence homology between the DNA56094 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 004974, the Incyte EST clone 004974 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 183 and is herein designated as DNA59214-1449 (SEQ ID NO:265).

The full length clone shown in Figure 183 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 42-44 and ending at the stop codon found at nucleotide positions 414-416 (Figure 183; SEQ ID NO:265). The predicted polypeptide precursor (Figure 184, SEQ ID NO:266) is 124 amino acids long. PRO1068 has a calculated molecular weight of approximately 14,284 daltons and an estimated pI of approximately 8.14. The PRO1068 polypeptide has the following additional features, as indicated in Figure 184: a signal peptide sequence at about amino acids 1-20, a urotensin II signature sequence at about amino acids 64-66, and a potential cAMP-and cGMP-dependent protein kinase phosphorylation site at about amino acids 112-115.

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An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 184 (SEQ ID NO:266), revealed homology between the PRO1068 amino acid sequence and the following Dayhoff sequences: HALBOP_1, MTV043_36,

150498, and P R78445

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Clone DNA59214-1449 was deposited with the ATCC on July 1, 1998 and is assigned ATCC deposit no.203046.

EXAMPLE 81: Isolation of cDNA clones Encoding Human PRO1066

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence designated herein as 79066. The Incyte EST cluster sequence no. 79066 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56121.

In light of an observed sequence homology between the DNA56121 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1515315, the Incyte EST clone 1515315 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 185 and is herein designated DNA59215-1425.

The full length clone shown in Figure 185 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 176-178 and ending at the stop codon found at nucleotide positions 527-529 (Figure 185; SEQ ID NO:267). The predicted polypeptide precursor is 117 amino acids long, has a calculated molecular weight of approximately 12,911 daltons and an estimated pI of approximately 5.46. Analysis of the full-length PRO1066 sequence shown in Figure 186 (SEQ ID NO:268) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 23, a cAMP- and cGMP-dependent protein kinase phosphorylation site from about amino acid 38 to about amino acid 41 and potential N-myristoylation sites from about amino acid 5 to about amino acid 10, from about amino acid 63 to about amino acid 68 and from about amino acid 83 to about amino acid 88. Clone UNQ524 (DNA59215-1425) has been deposited with the ATCC on June 9, 1998 and is assigned ATCC deposit no. 209961.

Analysis of the amino acid sequence of the full-length PRO1066 polypeptide suggests that it does not possess significant sequence similarity to any known human protein. However, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO1066 amino acid sequence and the following Dayhoff sequences, MOTI_HUMAN, AF025667_1, MTCY19H9_8 and RABIGKCH_1.

EXAMPLE 82: Isolation of cDNA Clones Encoding Human PRO1184

Use of the signal sequence algorithm described in Example 3 on ESTs from an Incyte database allowed identification a candidate sequence designated herein as DNA56375. This sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and

PCT/US99/12252 WO 99/63088

a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56375.

In light of an observed sequence homology between the DNA56375 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1428374, the Incyte EST clone 1428374 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 187.

The full length clone shown in Figure 187 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 106-108 and ending at the stop codon found at nucleotide positions 532-534 (Figure 187; SEQ ID NO:269). The predicted polypeptide precursor is 142 amino acids long, has a calculated molecular weight of approximately 15,690 daltons and an estimated pl of approximately 9.64. Analysis of the full-length PRO1184 sequence shown in Figure 188 (SEQ ID NO:270) evidences the presence of a signal peptide at about amino acids 1-38. Clone DNA59220-1514 has been deposited with the ATCC on June 9, 1998. It is understood that the deposited clone has the actual sequences and that representations are presented herein.

Analysis of the amino acid sequence of the full-length PRO1184 polypeptide suggests that it possesses some sequence identity with a protein called TIM from Drosophila virilis, designated "DVTIMS02_1" in the Dayhoff data base, (version 35.45 SwissProt 35). Other Dayhoff database (version 35.45 SwissProt 35) sequences having some degree of sequence identity with PRO1184 include: WIS1_SCHPO, F002186_1, ATAC00239124 and MSAIPRP_1.

EXAMPLE 83: Isolation of cDNA clones Encoding Human PRO1360

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST sequence from an Incyte database, designated DNA10572. This EST sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank, Merck/Wash. U.) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57314.

In light of an observed sequence homology between the DNA57314 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA406443, the Merck EST clone AA406443 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 189 and is herein designated as DNA59488-1603.

The full length clone shown in Figure 189 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 54-56 and ending at the stop codon found at nucleotide positions 909-911 (Figure 189; SEQ ID NO:271). The predicted polypeptide precursor (Figure 190, SEQ ID NO:272) is 285 amino acids long. PRO1360 has a calculated molecular weight of approximately 31,433 daltons and an estimated pI of approximately 7.32. Clone DNA59488-1603 was deposited with the ATCC on August 25, 1998 and is assigned ATCC deposit no. 203157.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 190 (SEQ ID NO:272), revealed sequence identity between the PRO1360 amino acid sequence and the following Dayhoff sequences: UN51_CAEEL, YD4B_SCHPO, AF000634_1, GFO_ZYMMO, YELJ_SCHPO, D86566_1, ZMGFO_1, S76976, PPSA SYNY3, and CEF28B1 4.

EXAMPLE 84: Isolation of cDNA clones Encoding Human PRO1029

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 18763. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57854.

In light of an observed sequence homology between the DNA57854 consensus sequence and an EST sequence encompassed within the Merck EST clone no. T98880, the Merck EST clone T98880 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 191 and is herein designated as DNA59493-1420.

Clone DNA59493-1420 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 39-41 and ending at the stop codon at nucleotide positions 297-299 (Figure 191). The predicted polypeptide precursor is 86 amino acids long (Figure 192). The full-length PRO1029 protein shown in Figure 192 has an estimated molecular weight of about 9,548 daltons and a pI of about 8.52. Analysis of the 30 full-length PRO1029 sequence shown in Figure 192 (SEQ ID NO:274) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19, an amino acid block having homology to bacterial rhodopsins retinal binding site protein from about amino acid 50 to about amino acid 61, a prenyl group binding site from about amino acid 83 to about amino acid 86 and a potential N-glycosylation site from about amino acid 45 to about amino acid 48. Clone DNA59493-1420 has been deposited with ATCC on July 1, 1998 and is assigned ATCC deposit no. 203050,

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 192 (SEQ ID NO:274), evidenced significant

homology between the PRO1029 amino acid sequence and the following Dayhoff sequences: S66088, AF031815_1, MM4A6L_1, PSEISS2a-1, S17699 and P_R63635.

EXAMPLE 85: Isolation of cDNA clones Encoding Human PRO1139

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 4461. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57312.

The DNA57312 consensus sequence included a 172 nucleotides long public EST (T62095, Merck/University of Washington public database). This EST clone, identified herein as a putative protein coding sequence, was purchased from Merck, and sequenced to provide the coding sequence of PRO1139 (Figure 193). As noted before, the deduced amino acid sequence of DNA59497-1496 shows a significant sequence identity with the deduced amino acid sequence of HSOBRGRP_1. The full-length protein (Figure 194) contains a putative signal peptide between amino acid residues 1 and about 28, and three putative transmembrane domains (approximate amino acid residues 33-52, 71-89, 98-120).

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EXAMPLE 86: Isolation of cDNA clones Encoding Human PRO1309

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed homology to SLIT.

RNA for construction of cDNA libraries was isolated from human fetall brain tissue. The cDNA libraries used to isolate the cDNA clones encoding human PRO1309 were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI.

The cDNA libraries (prepared as described above), were screened by hybridization with a synthetic oligonucleotide probe derived from the above described Incyte EST sequence:
5'-TCCGTGCAGGGGACGCCTTTCAGAAACTGCGCCGAGTTAAGGAAC-3' (SEQ ID NO:279).

A cDNA clone was isolated and sequenced in entirety. The entire nucleotide sequence of DNA59588-1571 is shown in Figure 195 (SEQ ID NO:277). Clone DNA59588-1571 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 720-722 and a stop codon at nucleotide positions 2286-2288 (Figure 195; SEQ ID NO:277). The predicted polypeptide precursor is 522 amino acids

long. The signal peptide is approximately at 1-34 and the transmembrane domain is at approximately 428-450 of SEQ ID NO:278. Clone DNA59588-1571 has been deposited with ATCC and is assigned ATCC deposit no. 203106. The full-length PRO1309 protein shown in Figure 196 has an estimated molecular weight of about 58,614 daltons and a pI of about 7.42.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 196 (SEQ ID NO:278), revealed sequence identity between the PRO1309 amino acid sequence and the following Dayhoff sequences: AB007876_1, GPV_MOUSE, ALS_RAT, P_R85889, LUM_CHICK, AB014462_1, PGS1_CANFA, CEM88_7, A58532 and GEN11209.

EXAMPLE 87: Isolation of cDNA Clones Encoding Human PRO1028

Use of the signal sequence algorithm described in Example 3 above allowed identification of a certain EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA59603.

In light of an observed sequence homology between the DNA59603 sequence and an EST sequence contained within Incyte EST clone no. 1497725, the Incyte EST clone no. 1497725 was purchased and the cDNA insert was obtained and sequenced. It was found that the insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 197 and is herein designated as DNA59603-1419.

The entire nucleotide sequence of DNA59603-1419 is shown in Figure 197 (SEQ ID NO:280). Clone DNA59603-1419 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 21-23 and ending at the stop codon at nucleotide positions 612-614 (Figure 197). The predicted polypeptide precursor is 197 amino acids long (Figure 198). The full-length PRO1028 protein shown in Figure 198 has an estimated molecular weight of about 20,832 daltons and a pl of about 8.74. Clone DNA59603-1419 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:281, the putative signal peptide is at about amino acids 1-19 of SEQ ID NO:281. An N-glycosylation site is at about amino acids 35-38 of SEQ ID NO:281. A C-type lectin domain is at about amino acids 108-117 of SEQ ID NO:281, indicating that PRO513 may be related to or be a lectin. The corresponding nucleotides of these amino acid sequences or others can be routinely determined given the sequences provided herein.

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EXAMPLE 88: Isolation of cDNA Clones Encoding Human PRO1027

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a certain EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56399.

In light of an observed sequence homology between the DNA56399 sequence and an EST sequence contained within Incyte EST clone no. 937605, the Incyte EST clone no. 937605 was purchased and the cDNA insert was obtained and sequenced. It was found that the insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 199 and is herein designated as DNA59605-1418.

The entire nucleotide sequence of DNA59605-1418 is shown in Figure 199 (SEQ ID NO:282). Clone DNA59605-1418 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 31-33 and ending at the stop codon at nucleotide positions 262-264 (Figure 199). The predicted polypeptide precursor is 77 amino acids long (Figure 200). The full-length PRO1027 protein shown in Figure 200 has an estimated molecular weight of about 8,772 daltons and a pI of about 9.62. Clone DNA59605-1418 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:283, the putative signal peptide is at about amino acids 1-33 of SEQ ID NO:283. The type II fibronectin collagen-binding domain begins at about amino acid 30 of SEQ ID NO:283. The corresponding nucleotides for these amino acid sequences and others can be routinely determined given the sequences provided herein. PRO1027 may be involved in tissue formation or repair.

The following Dayhoff designations appear to have some sequence identity with PRO1027: SFT2_YEAST; ATM3E9_2; A69826; YM16_MARPO; E64896; U60193_2; MTLRAJ205_1; MCU60315_70; SPAS_SHIFL; and S54213.

EXAMPLE 89: Isolation of cDNA Clones Encoding Human PRO1107

Use of the signal sequence algorithm described in Example 3 above allowed identification of a certain EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence

PCT/US99/12252 WO 99/63088

obtained therefrom is herein designated DNA56402.

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In light of an observed sequence homology between the DNA56402 sequence and an EST sequence contained within Incyte EST clone no. 3203694, the Incyte EST clone no. 3203694 was purchased and the cDNA insert was obtained and sequenced. It was found that the insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 201 and is herein designated as DNA59606-1471.

The entire nucleotide sequence of DNA59606-1471 is shown in Figure 201 (SEQ ID NO:284). Clone DNA59606-1471 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 244-246 and ending at the stop codon at nucleotide positions 1675-1677 of SEQ ID NO:284 (Figure 201). The predicted polypeptide precursor is 477 amino acids long (Figure 202). The full-length PRO1107 protein shown in Figure 202 has an estimated molecular weight of about 54,668 daltons and a pl of about 6.33. 10 Clone DNA59606-1471 has been deposited with ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO1107 polypeptide suggests that it possesses significant sequence similarity to phosphodiesterase I/nucleotide phyrophosphatase, human insulin receptor tyrosine kinase inhibitor, alkaline phosphodiesterase and autotaxin, thereby indicating that PRO1107 may have at least one or all of the activities of these proteins, and that PRO1107 is a novel phosphodiesterase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO1107 amino acid sequence and at least the following Dayhoff sequences: AF005632_1, P R79148, RNU78787 1, AF060218_4, A57080 and HUMATXT_1.

EXAMPLE 90: Isolation of cDNA clones Encoding Human PRO1140

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence, Incyte cluster sequence No. 135917. This sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary 25 EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56416.

In light of an observed sequence homology between DNA56416 and an EST sequence contained within Incyte EST clone no. 3345705, Incyte EST clone no. 3345705 was obtained and its insert sequenced. It was found that the insert encoded a full-length protein The sequence, designated herein as DNA59607-1497, which is shown in Figure 203, is the full-length DNA sequence for PRO1140. Clone DNA59607-1497 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209946.

The entire nucleotide sequence of DNA59607-1497 is shown in Figure 203 (SEQ ID NO:286). Clone DNA59607-1497 contains a single open reading frame with an apparent translational initiation site at nucleotide

positions 210-212 and ending at the stop codon at nucleotide positions 975-977 (Figure 203). The predicted polypeptide precursor is 255 amino acids long (Figure 204). The full-length PRO1140 protein shown in Figure 204 has an estimated molecular weight of about 29,405 daltons and a pI of about 7.64. Analysis of the full-length PRO1140 sequence shown in Figure 204 (SEQ ID NO:287) evidences the presence of three transmembrane domains at about amino acids 101 to 118, 141 to 161 and 172 to 191.

Analysis of the amino acid sequence of the full-length PRO1140 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1140 amino acid sequence and the following Dayhoff sequences: AF023602_1, AF000368_1, CIN3_RAT, AF003373_1, GEN13279, and AF003372_1.

Clone DNA59607-1497 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209946.

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EXAMPLE 91: Isolation of cDNA clones Encoding Human PRO1106

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence. This sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56423.

In light of an observed sequence homology between DNA56423 and an EST sequence contained within Incyte EST clone no. 1711247, Incyte EST clone no. 1711247 was obtained and its insert sequenced. It was found that the insert encoded a full-length protein The sequence, designated herein as DNA59609-1470, which is shown in Figure 205, is the full-length DNA sequence for PRO1106. Clone DNA59609-1470 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209963.

The entire nucleotide sequence of DNA59609-1470 is shown in Figure 205 (SEQ ID NO:288). Clone DNA59609-1470 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 61-63 and ending at the stop codon at nucleotide positions 1468-1470 of SEQ ID NO:288 (Figure 205). The predicted polypeptide precursor is 469 amino acids long (Figure 206). The full-length PRO1106 protein shown in Figure 206 has an estimated molecular weight of about 52,689 daltons and a pI of about 8.68. It is understood that the skilled artisan can construct the polypeptide or nucleic acid encoding therefor to exclude any one or more of all of these domains. For example, the transmembrane domain region(s) and/or either of the amino terminal or carboxyl end can be excluded. Clone DNA59609-1470 has been deposited with ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO1106 polypeptide suggests that it possesses significant sequence similarity to the peroxisomal ca-dependent solute carrier, thereby indicating that PRO1106

may be a novel transporter. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO1106 amino acid sequence and at least the following Dayhoff sequences, AF004161 1, IG002N01 25, GDC BOVIN and BT1 MAIZE.

EXAMPLE 92: Isolation of cDNA clones Encoding Human PRO1291

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 120480. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56425.

In light of an observed sequence homology between the DNA56425 sequence and an EST sequence encompassed within the Incyte EST clone no. 2798803, the Incyte EST clone 2798803 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 207 and is herein designated as DNA59610-1556.

Clone DNA59610-1556 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 61-63 and ending at the stop codon at nucleotide positions 907-909 (Figure 207). The predicted polypeptide precursor is 282 amino acids long (Figure 208). The full-length PRO1291 protein shown in Figure 208 has an estimated molecular weight of about 30,878 daltons and a pl of about 5.27. Analysis of the full-length PRO1291 sequence shown in Figure 208 (SEQ ID NO:291) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, a transmembrane domain from about amino acid 258 to about amino acid 281 and potential N-glycosylation sites from about amino acid 112 to about amino acid 115, from about amino acid 160 to about amino acid 163, from about amino acid 190 to about amino acid 193, from about amino acid 216 to about amino acid 219 and from about amino acid 220 to about amino acid 223.. Clone DNA59610-1556 has been deposited with ATCC on June 16, 1998 and is assigned ATCC deposit no. 209990.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 208 (SEQ ID NO:291), evidenced significant homology between the PRO1291 amino acid sequence and the following Dayhoff sequences: HSU90552_1, HSU90144_1, AF033107_1, HSB73_1, HSU90142_1, GGCD80_1, P_W34452, MOG_MOUSE, B39371 and P_R71360.

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EXAMPLE 93: Isolation of cDNA clones Encoding Human PRO1105

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56430.

In light of an observed sequence homology between the DNA56430 sequence and an EST sequence encompassed within the Incyte EST clone no. 1853047, the Incyte EST clone 1853047 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 209 and is herein designated as DNA59612-1466.

The entire nucleotide sequence of DNA59612-1466 is shown in Figure 209 (SEQ ID NO:292). Clone DNA59612-1466 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 28-30 and ending at the stop codon at nucleotide positions 568-570 of SEQ ID NO:292 (Figure 209). The predicted polypeptide precursor is 180 amino acids long (Figure 210). The full-length PRO1105 protein shown in Figure 210 has an estimated molecular weight of about 20,040 daltons and a pI of about 8.35. Clone DNA59612-1466 has been deposited with the ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 210, a signal peptide is at about amino acids 1-19 of SEQ ID NO:293 and transmembrane domains are shown at about amino acids 80-99 and 145-162 of SEQ ID NO:293. It is understood that the skilled artisan could form a polypeptide with all of or any combination or individual selection of these regions. It is also understood that the corresponding nucleic acids can be routinely identified and prepared based on the information provided herein.

EXAMPLE 94: Isolation of cDNA clones Encoding Human PRO511

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56434.

In light of an observed sequence homology between the DNA56434 sequence and an EST sequence encompassed within the Incyte EST clone no. 1227491, the Incyte EST clone 1227491 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 211 and is herein designated as DNA59613-1417.

The entire nucleotide sequence of DNA59613-1417 is shown in Figure 211 (SEQ ID NO:294). Clone DNA59613-1417 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 233-235 and ending at the stop codon at nucleotide positions 944-946 (Figure 211). The predicted polypeptide precursor is 237 amino acids long (Figure 212). The full-length PRO511 protein shown in Figure 212 has an estimated molecular weight of about 25,284 daltons and a pl of about 5.74. Clone DNA59613-1417 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:295, the putative signal peptide is at about amino acids 1-25 of SEQ ID NO:295. The N-glycosylation sites are at about amino acids 45-48, 73-76, 107-110, 118-121, 132-135, 172-175, 175-178 and 185-188 of SEQ ID NO:295. An arthropod defensins conserved region is at about amino acids 176-182 of SEQ ID NO:295. A kringle domain begins at about amino acid 128 of SEQ ID NO:295 and a ly-6/u-PAR domain begins at about amino acid 6 of SEQ ID NO:295. The corresponding nucleotides of these amino acid sequences and others can be routinely determined given the sequences provided herein.

The designations appearing in a Dayhoff database with which PRO511 has some sequence identity are as follows: SSC20F10_1; SF041083; P_W26579; S44208; JC2394; PSTA_DICDI; A27020; S59310; RAG1_RABIT; and MUSBALBC1_1.

EXAMPLE 95: Isolation of cDNA clones Encoding Human PRO 1 104

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56446.

In light of an observed sequence homology between the DNA56446 sequence and an EST sequence encompassed within the Incyte EST clone no. 2837496, the Incyte EST clone 2837496 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 213 and is herein designated as DNA59616-1465.

The entire nucleotide sequence of DNA59616-1465 is shown in Figure 213 (SEQ ID NO:296). Clone DNA59616-1465 contains a single open reading frame with an apparent translational initiation site at nucleotide

positions 109-111 and ending at the stop codon at nucleotide positions 1132-1134 of SEQ ID NO:296 (Figure 213). The predicted polypeptide precursor is 341 amino acids long (Figure 214). The full-length PRO1104 protein shown in Figure 214 has an estimated molecular weight of about 36,769 daltons and a pI of about 9.03. Clone DNA59616-1465 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 214, a signal peptide is at about amino acids 1-22 of SEQ ID NO:297. N-myristoylation sites are at about amino acids 41-46, 110-115, 133-138, 167-172 and 179-184 of SEQ ID NO:297.

10 EXAMPLE 96: Isolation of cDNA clones Encoding Human PRO1100

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

In light of an observed sequence homology between the obtained consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2305379, the Incyte EST clone 2305379 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 215 and is herein designated as DNA59619-1464.

The entire nucleotide sequence of DNA59619-1464 is shown in Figure 215 (SEQ ID NO:298). Clone DNA59619-1464 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 33-35 and ending at the stop codon at nucleotide positions 993-995 of SEQ ID NO:298 (Figure 215). The predicted polypeptide precursor is 320 amino acids long (Figure 216). The full-length PRO1100 protein shown in Figure 216 has an estimated molecular weight of about 36,475 daltons and a pI of about 7.29. Clone DNA59619-1464 has been deposited with ATCC on July 1, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Upon analyzing SEQ ID NO:299, the approximate locations of the signal peptide, the transmembrane domains, an N-glycosylation site, an N-myristoylation site, a CUB domain and an amiloride-sensitive sodium channel domain are present. It is believed that PRO1100 may function as a channel. The corresponding nucleic acids for these amino acids and others can be routinely determined given SEQ ID NO:299..

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EXAMPLE 97: Isolation of cDNA clones Encoding Human PRO836

WO 99/63088

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained is herein designated DNA56453.

In light of an observed sequence homology between the DNA56453 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2610075, the Incyte EST clone 2610075 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 217 and is herein designated as DNA59620-1463.

The entire nucleotide sequence of DNA59620-1463 is shown in Figure 217 (SEO ID NO:300). Clone DNA59620-1463 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 65-67 and ending at the stop codon at nucleotide positions 1448-1450 of SEQ ID NO:300 (Figure 217). The predicted polypeptide precursor is 461 amino acids long (Figure 218). The full-length PRO836 protein shown in Figure 218 has an estimated molecular weight of about 52,085 daltons and a pl of about 5.36. Analysis of the full-length PRO836 sequence shown in Figure 218 (SEQ ID NO:301) evidences the presence of the following: a signal peptide, N-glycosylation sites, N-myristoylation sites, a domain conserved in the YJL126w/YLR351c/yhcX family of proteins, and a region having sequence identity with SLS1. Clone DNA59620-1463-has-been-deposited-with-ATCC-on-June-16,-1998.-It-is understood-that-the-deposited-clonehas the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO836 polypeptide suggests that it possesses some sequence similarity to SLS1, thereby indicating that PRO836 may be involved in protein translocation of the ER. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some homology between the PRO836 amino acid sequence and at least the following Dayhoff sequences, SS8132, SPBC3B9_1, S66714, CRU40057_1 and IMA_CAEEL.

EXAMPLE 98: Isolation of cDNA clones Encoding Human PRO1141

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 11873. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or

PCT/US99/12252 WO 99/63088

in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56518.

In light of an observed sequence homology between the DNA56518 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2679995, the Incyte EST clone 2679995 was purchased 5 and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 219 and is herein designated as DNA59625-1498.

Clone DNA59625-1498 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 204-206 and ending at the stop codon at nucleotide positions 945-947 (Figure 219). The predicted polypeptide precursor is 247 amino acids long (Figure 220). The full-length PRO1141 protein shown in Figure 220 has an estimated molecular weight of about 26,840 daltons and a pl of about 8.19. Analysis 10 of the full-length PRO1141 sequence shown in Figure 220 (SEQ ID NO:303) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19 and transmembrane domains from about amino acid 38 to about amino acid 57, from about amino acid 67 to about amino acid 83, from about amino acid 117 to about amino acid 139 and from about amino acid 153 to about amino acid 170. Clone DNA59625-1498 has been deposited with ATCC on June 16, 1998 and is assigned ATCC deposit no. 209992.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 220 (SEQ ID NO:303), evidenced significant homology between the PRO1141 amino acid sequence and the following Dayhoff sequences: CEVF36H2L_2, PCRB7PRJ_1, AB000506_1, LEU95008_1, MRU87980_15, YIGM_ECOLI, STU65700_1, GHU62778_1, CYST_SYNY3 and AF009567 1.

EXAMPLE 99: Isolation of cDNA clones Encoding Human PRO1132

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A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as DNA35934. Based on the DNA35934 25 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1132.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-TCCTGTGACCACCCCTCTAACACC-3' (SEQ ID NO:310) and

reverse PCR primer: 5'-CTGGAACATCTGCTGCCCAGATTC-3' (SEQ ID NO:311).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus sequence which had the following nucleotide sequence:

5'-GTCGGATGACAGCAGCAGCCGCATCATCAATGGATCCGACTGCGATATGC-3' (SEQ ID NO:312).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was 35 screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1132 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1132 and the derived protein sequence for PRO1132.

The entire nucleotide sequence of PRO1132 is shown in Figure 225 (SEQ ID NO:308). Clone DNA59767-1489 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 354-356 and a stop codon at nucleotide positions 1233-1235 (Figure 225; SEQ ID NO:308). The predicted polypeptide precursor is 293 amino acids long. The signal peptide is at about amino acids 1-22 and the histidine active site is at about amino acids 104-109 of SEQ ID NO:309. Clone DNA59767-1489 has been deposited with ATCC (having the actual sequence rather than representations based on sequencing techniques as presented herein) and is assigned ATCC deposit no. 203108. The full-length PRO1132 protein shown in Figure 226 has an estimated molecular weight of about 32,020 daltons and a pI of about 8.7.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 226 (SEQ ID NO:309), revealed sequence identity between the PRO1132 amino acid sequence and the following Dayhoff sequences: SSU76256_1, P_W10694, MMAE000663_6, AF013988_1, U66061_8, MMAE000665_2, MMAE00066415, MMAE00066414, MMAE000665_4 and MMAE00066412.

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EXAMPLE 100: Isolation of cDNA clones Encoding Human NL7 (PRO1346)

A single EST sequence (#1398422) was found in the LIFESEQ^e database as described in Example 1 above. This EST sequence was renamed as DNA45668. Based on the DNA45668 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for NL7.

PCR primers (forward and reverse) were synthesized:

forward-PCR-primer: -5'-CACACGTCCAACCTCAATGGGCAG-3'-(SEQ-ID-NO:315)

reverse PCR primer: 5'-GACCAGCAGGGCCAAGGACAAGG-3' (SEQ ID NO:316)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45668 sequence which had the following nucleotide sequence:

hybridization probe:

5'-GTTCTCTGAGATGAAGATCCGGCCGGTCCGGGAGTACCGCTTAG-3' (SEO ID NO:317)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the NL7 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from a human fetal kidney library (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for NL7 (designated herein as DNA59776-1600 [Figure 227, SEQ ID NO:313]) and the derived protein sequence for NL7 (PRO1346).

The entire coding sequence of NL7 (PRO1346) is shown in Figure 227 (SEQ ID NO:313). Clone DNA59776-1600 contains a single open reading frame with an apparent translational initiation site at nucleotide

positions 1-3 and an apparent stop codon at nucleotide positions 1384-1386. The predicted polypeptide precursor is 461 amino acids long. The protein contains an apparent type II transmembrane domain at amino acid positions from about 31 to about 50; fibrinogen beta and gamma chains C-terminal domain signature starting at about amino acid position 409, and a leucine zipper pattern starting at about amino acid positions 140, 147, 154 and 161, respectively. Clone DNA59776-1600 has been deposited with ATCC and is assigned ATCC deposit no. 203128. The full-length NL7 protein shown in Figure 228 has an estimated molecular weight of about 50,744 daltons and a pl of about 6.38.

Based on a WU-BLAST2 sequence alignment analysis (using the WU-BLAST2 computer program) of the full-length sequence, NL7 shows significant amino acid sequence identity to a human microfibril-associated glycoprotein (1 MFA4_HUMAN); to known TIE-2 ligands and ligand homologues, ficolin, serum lectin and TGF-1 binding protein.

EXAMPLE 101: Isolation of cDNA clones Encoding Human PRO1131

A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated DNA43546 (see Figure 231; SEQ ID NO:320). The DNA43546 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA45627.

Based on the DNA45627 sequence, oligonucleotide probes were generated and used to screen a human library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the Sfil site; see, Holmes et al., Science 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and 2 reverse) were synthesized:

forward PCR primer 5'-ATGCAGGCCAAGTACAGCAGCAC-3' (SEQ ID NO:321);

reverse PCR primer 1 5'-CATGCTGACGACTTCCTGCAAGC-3' (SEQ ID NO:322); and

reverse PCR primer 1 5'-CCACACAGTCTCTGCTTCTTGGG-3' (SEQ ID NO:323)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA45627 sequence which had the following nucleotide sequence:

hybridization probe

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5'-ATGCTGGATGATGGGGACACCACCATGAGCCTGCATT-3' (SEQ ID NO:324).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1131 gene using the probe oligonucleotide and one of the PCR primers.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 144-146, and a stop signal at nucleotide positions 984-986 (Figure 229; SEQ ID NO:318). The predicted polypeptide precursor is 280 amino acids long, has a calculated molecular weight of approximately 31,966 daltons and an estimated pl of approximately 6.26. The transmembrane domain sequence is at about 49-74 of SEQ ID NO:319 and the region having sequence identity with LDL receptors is about 50-265 of SEQ ID NO:319. PRO1131 contains potential N-linked glycosylation sites at amino acid positions 95-98 and 169-172 of SEQ ID NO:319. Clone DNA59777-1480 has been deposited with the ATCC and is assigned ATCC deposit no. 203111.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 230 (SEQ ID NO:319), evidenced some sequence identity between the PRO1131 amino acid sequence and the following Dayhoff sequences: AB010710_1, I49053, I49115, RNU56863_1, LY4A_MOUSE, I55686, MMU56404_1, I49361, AF030313_1 and MMU09739_1.

EXAMPLE 102: Isolation of cDNA clones Encoding Human PRO1281

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as DNA35720. Based on the DNA35720 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1281.

PCR primers (forward and reverse) were synthesized:

forward PCR primers:

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- 20 5'-TGGAAGGCTGCCGCAACGACAATC-3' (SEQ ID NO:327);
 - 5'-CTGATGTGGCCGATGTTCTG-3' (SEQ ID NO:328); and
 - 5'-ATGGCTCAGTGTGCAGACAG-3'-(SEQ-ID-NO:329);-

reverse PCR primers:

- 5'-GCATGCTCCGTGAAGTAGTCC-3' (SEQ ID NO:330); and
- 25 5'-ATGCATGGGAAAGAAGGCCTGCCC-3' (SEQ ID NO:331).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA35720 sequence which had the following nucleotide sequence:

hybridization probe:

- 5'-TGCACTGGTGACCACGAGGGGGTGCACTATAGCCATCTGGAGCTGAG-3' (SEQ ID NO:332).
- In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO1281 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated human fetal liver.
- DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1281 (designated herein as DNA59820-1549 [Figure 232, SEQ ID NO:325]; and the derived protein sequence for PRO1281.

PCT/US99/12252 WO 99/63088

The entire coding sequence of PRO1281 is shown in Figure 232 (SEQ ID NO:325). Clone DNA59820-1549 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 228-230 and an apparent stop codon at nucleotide positions 2553-2555. The predicted polypeptide precursor is 775 amino acids long. The full-length PRO1281 protein shown in Figure 233 has an estimated molecular weight of about 85,481 daltons and a pI of about 6.92. Additional features include a signal peptide at about amino acids 1-15; and potential N-glycosylation sites at about amino acids 138-141 and 361-364.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 233 (SEQ ID NO:326), revealed some sequence identity between the PRO1281 amino acid sequence and the following Dayhoff sequences: S44860, CET24D1_1, CEC38H2_3, CAC2_HAECO, B3A2_HUMAN, S22373, CEF38A3_2, CEC34F6_2, CEC34F6_3, and 10 CELT22B11_3.

Clone DNA59820-1549 has been deposited with ATCC and is assigned ATCC deposit no. 203129.

EXAMPLE 103: Isolation of cDNA clones Encoding Human PRO1064

A cDNA sequence isolated in the amylase screen described in Example 2 above was found, by the WU-BLAST2 sequence alignment computer program, to have no significant sequence identity to any known human protein. This cDNA sequence is herein designated DNA45288. The DNA45288 sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater 20 that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is herein designated DNA48609. Oligonucleotide primers based upon the DNA48609 sequence were then synthesized and employed to screen a human fetal kidney cDNA library which resulted in the identification of the DNA59827-1426 clone shown in Figure 234. The cloning vector was pRK5B (pRK5B is a precursor of 25 pRK5D that does not contain the Sfil site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

The oligonucleotide probes employed were as follows:

forward PCR primer 5'-CTGAGACCCTGCAGCACCATCTG-3' (SEQ ID NO:336)

reverse PCR primer 5'-GGTGCTTCTTGAGCCCCACTTAGC-3' (SEQ ID NO:337) 30

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA48609 sequence which had the following nucleotide sequence

hybridization probe

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5'-AATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCCGCTGT-3' (SEQ ID NO:338)

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 532-534 and a stop signal at nucleotide positions 991-993 (Figure 234, SEQ ID NO:333). The predicted polypeptide precursor is 153 amino acids long, has a calculated

molecular weight of approximately 17,317 daltons and an estimated pI of approximately 5.17. Analysis of the full-length PRO1064 sequence shown in Figure 235 (SEQ ID NO:334) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, a transmembrane domain from about amino acid 89 to about amino acid 110, an indole-3-glycerol phosphate synthase homology block from about amino acid 74 to about amino acid 105 and a Myb DNA binding domain protein repeat protein homology block from about amino acid 114 to about amino acid 137. Clone DNA59827-1426 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203089.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 235 (SEQ ID NO:334), evidenced homology between the PRO1064 amino acid sequence and the following Dayhoff sequences: MMNP15PRO_1, BP187PLYH_1, CELF42G8_4, MMU58888_1, GEN14270, TUB8_SOLTU, RCN_MOUSE, HUMRBSY79_1, SESENODA 1 and A21467 1.

EXAMPLE 104: Isolation of cDNA clones Encoding Human PRO1379

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein DNA45232. Based on the DNA45232 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1379.

PCR primers (forward and reverse) were synthesized:

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20 forward PCR primer 5'-TGGACACCGTACCCTGGTATCTGC-3' (SEQ ID NO:341)
reverse PCR primer 5'-CCAACTCTGAGGAGAGCAAGTGGC-3' (SEQ ID NO:342)

Additionally, a synthetic oligonucleotide hybridization-probe-was-constructed-from-the-consensus DNA45232 sequence which had the following nucleotide sequence:

hybridization probe

25 5'-TGTATGTGCACACCCTCACCATCACCTCCAAGGGCAAGGAGAAC-3' (SEQ ID NO:343).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1379 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1379 which is designated herein as DNA59828-1608 and shown in Figure 237 (SEQ ID NO:339); and the derived protein sequence for PRO1379 (SEQ ID NO:340).

The entire coding sequence of PRO1379 is shown in Figure 237 (SEQ ID NO:339). Clone DNA59828-1608 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 10-12 and an apparent stop codon at nucleotide positions 1732-1734. The predicted polypeptide precursor is 574 amino acids long. The full-length PRO1379 protein shown in Figure 238 has an estimated molecular weight of about 65,355 daltons and a pI of about 8.73. Additional features include a signal peptide at about amino acids

1-17 and potential N-glycosylation sites at about amino acids 160-163, 287-290, and 323-326.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 238 (SEQ ID NO:340), revealed some homology between the PRO1379 amino acid sequence and the following Dayhoff sequences: YHY8_YEAST, AF040625_1, HP714394_1, and HIV18U45630_1.

Clone DNA59828-1608 has been deposited with ATCC and is assigned ATCC deposit no. 203158.

EXAMPLE 105: Isolation of cDNA Clones Encoding Human PRO844

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An expressed sequence tag (EST) DNA database (LIFESEQTM, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed sequence identity with aLP. Based on the information and discoveries provided herein, the clone for this EST, Incyte clone no. 2657496 from a cancerous lung library was further examined.

DNA sequencing of the insert for this clone gave a sequence (herein designated as DNA59838-1462; SEQ ID NO:344) which includes the full-length DNA sequence for PRO844 and the derived protein sequence for PRO844.

The entire nucleotide sequence of DNA59838-1462 is shown in Figure 239 (SEQ ID NO:344). Clone DNA59838-1462 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 5-7 and ending at the stop codon at nucleotide positions 338-340 of SEQ ID NO:344 (Figure 239). The predicted polypeptide precursor is 111 amino acids long (Figure 240). The full-length PRO844 protein shown in Figure 240 has an estimated molecular weight of about 12,050 daltons and a pl of about 5.45. Clone UNQ544 DNA59838-1462 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO844 polypeptide suggests that it possesses significant sequence similarity to serine protease inhibitors, thereby indicating that PRO844 may be a novel proteinase inhibitor. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO844 amino acid sequence and at least the following Dayhoff sequences, ALK1_HUMAN, P_P82403, P_P82402, ELAF_HUMAN and P_P60950.

EXAMPLE 106: Isolation of cDNA Clones Encoding Human PRO848

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence

obtained therefrom is herein designated DNA55999.

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In light of an observed sequence homology between the DNA55999 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2768571, the Incyte EST clone 2768571 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 241 and is herein designated as DNA59839-1461.

The entire nucleotide sequence of DNA59839-1461 is shown in Figure 241 (SEQ ID NO:346). Clone DNA59839-1461 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 146-148 and ending at the stop codon at nucleotide positions 1946-1948 of SEQ ID NO:346 (Figure 241). The predicted polypeptide precursor is 600 amino acids long (Figure 242). The full-length PRO848 protein shown in Figure 242 has an estimated molecular weight of about 68,536 daltons. Clone DNA59839-1461 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO848 polypeptide suggests that it may be a novel sialyltransferase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO848 amino acid sequence and at least the following Dayhoff sequences, P_R78619 (GalNAc-alpha-2, 6-sialyltransferase), CAAG5_CHICK (alpha-n-acetylgalactosamide alpha-2, 6-sialyltransferase), HSU14550_1,CAG6_HUMAN and P_R63217 (human alpha-2, 3-sialyltransferase).

EXAMPLE 107: Isolation of cDNA Clones Encoding Human PRO1097

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST-DNA database (LIFESEQ[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56006.

In light of an observed sequence homology between the DNA56006 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2408105, the Incyte EST clone 2408105 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 243 and is herein designated as DNA59841-1460.

The entire nucleotide sequence of DNA59841-1460 is shown in Figure 243 (SEQ ID NO:348). Clone DNA59841-1460 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 3-5 and ending at the stop codon at nucleotide positions 276-278 of SEQ ID NO:348 (Figure 243). The predicted polypeptide precursor is 91 amino acids long (Figure 244). The full-length PRO1097 protein shown in Figure 244 has an estimated molecular weight of about 10,542 daltons and a pI of about 10.04. Clone DNA59841-1460 has been deposited with ATCC on July 1, 1998. It is understood that the deposited clone has

PCT/US99/12252 WO 99/63088

the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 244, the signal peptide is at about amino acids 1-20 of SEQ ID NO:349. The glycoprotease family protein domain starts at about amino acid 56, and the acyltransferase ChoActase/COT/CPT family peptide starts at about amino acid 49 of SEQ ID NO:349.

EXAMPLE 108: Isolation of cDNA clones Encoding Human PRO1153

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56008.

In light of an observed sequence homology between the DNA56008 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2472409, the Incyte EST clone 2472409 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 245 and is herein designated as DNA59842-1502.

The full length clone shown in Figure 245 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 92-94 and ending at the stop codon found at nucleotide positions 683-685 (Figure 245; SEQ ID NO:350). The predicted polypeptide precursor (Figure 246, SEQ ID NO:351) is 197 amino acids long. PRO1153 has a calculated molecular weight of approximately 21,540 daltons and an estimated pI of approximately 8.31. Clone DNA59842-1502 has been deposited with ATCC and is assigned 25 ATCC deposit no. 209982. It is understood that the correct and actual sequence is in the deposited clone while herein are present representations based on current sequencing techniques which may have minor errors.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the fulllength sequence, PRO1153 shows some amino acid sequence identity to the following Dayhoff designations: S57447; SOYHRGPC_1; S46965; P_P82971; VCPHEROPH_1; EXTN_TOBAC; MLCB2548_9; ANXA_RABIT; JC5437 and SSGP_VOLCA.

EXAMPLE 109: Isolation of cDNA clones Encoding Human PRO1154

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in

Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56025.

In light of an observed sequence homology between the DNA56025 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2169375, the Incyte EST clone 2169375 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 247 and is herein designated as DNA59846-1503.

The full length clone shown in Figure 247 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 86-88 and ending at the stop codon found at nucleotide positions 2909-2911 (Figure 247; SEQ ID NO:352). The predicted polypeptide precursor (Figure 248, SEQ ID NO:353) is 941 amino acids long. PRO1154 has a calculated molecular weight of approximately 107,144 daltons and an estimated pI of approximately 6.26. Clone DNA59846-1503 has been deposited with ATCC and is assigned ATCC deposit no. 209978.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1154 shows sequence identity to at least the following Dayhoff designations: AB011097_1, AMPN_HUMAN, RNU76997_1, 159331, GEN14047, HSU62768_1, P_R51281, CET07F10_1, SSU66371_1, and AMPRE_HUMAN.

EXAMPLE 110: Isolation of cDNA clones Encoding Human PRO1181

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database, designated herein as 82468. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56029.

In light of an observed sequence homology between the DNA56029 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2186536, the Incyte EST clone 2186536 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 249 and is herein designated as DNA59847-1511.

Clone DNA59847-1511 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 17-19 and ending at the stop codon at nucleotide positions 1328-1330 (Figure 249). The predicted polypeptide precursor is 437 amino acids long (Figure 250). The full-length PRO1181 protein shown in Figure 250 has an estimated molecular weight of about 46,363 daltons and a pI of about 6.22. Analysis of the full-length PRO1181 sequence shown in Figure 250 (SEQ ID NO:355) evidences the presence of the

following: a signal peptide from about amino acid 1 to about amino acid 15, potential N-glycosylation sites from about amino acid 46 to about amino acid 49, from about amino acid 189 to about amino acid 192 and from about amino acid 382 to about amino acid 385 and amino acid sequence blocks having homology to Ly-6/u-PAR domain proteins from about amino acid 287 to about amino acid 300 and from about amino acid 98 to about amino acid 111. Clone DNA59847-1511 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203098.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 250 (SEQ ID NO:355), evidenced homology between the PRO1181 amino acid sequence and the following Dayhoff sequences: AF041083_1, P_W26579, RNMAGPIAN_1, CELT13C2_2, LMSAP2GN_1, S61882, CEF35C5_12, DP87_DICDI, GIU47631_1 and P R07092.

EXAMPLE 111: Isolation of cDNA clones Encoding Human PRO1182

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database, designated herein as 146647. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56033.

In light of an observed sequence homology between the DNA56033 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2595195, the Incyte EST clone 2595195 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 251 and is herein designated as DNA59848-1512.

Clone DNA59848-1512 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 67-69 and ending at the stop codon at nucleotide positions 880-882 (Figure 251). The predicted polypeptide precursor is 271 amino acids long (Figure 252). The full-length PRO1182 protein shown in Figure 252 has an estimated molecular weight of about 28,665 daltons and a pI of about 5.33. Analysis of the full-length PRO1182 sequence shown in Figure 252 (SEQ ID NO:357) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25, an amino acid block having homology to C-type lectin domain proteins from about amino acid 247 to about amino acid 256 and an amino acid sequence block having homology to C1q domain proteins from about amino acid 44 to about amino acid 77. Clone DNA59848-1512 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203088.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 252 (SEQ ID NO:357), evidenced significant

homology between the PRO1182 amino acid sequence and the following Dayhoff sequences: PSPD_BOVIN, CL43_BOVIN, CONG_BOVIN, P_W18780, P_R45005, P_R53257 and CELEGAP7 1.

EXAMPLE 112: Isolation of cDNA clones Encoding Human PRO1155

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56102.

In light of an observed sequence homology between the DNA56102 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2858870, the Incyte EST clone 2858870 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 253 and is herein designated as DNA59849-1504.

The full length clone shown in Figure 253 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 158-160 and ending at the stop codon found at nucleotide positions 563-565 (Figure 253; SEQ ID NO:358). The predicted polypeptide precursor (Figure 254, SEQ ID NO:359) is 135 amino acids long. PRO1155 has a calculated molecular weight of approximately 14,833 daltons and an estimated pI of approximately 9.78. Clone DNA59849-1504 has been deposited with ATCC and is assigned ATCC deposit no. 209986. It is understood that the actual clone has the correct sequence whereas herein are only representations which are prone to minor sequencing errors.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1155 shows some amino acid sequence identity with the following Dayhoff designations: TKNK_BOVIN; PVB19X587_1; AF019049_1; P_W00948; S72864; P_W00949; I62742; AF038501_1; TKNG_HUMAN; and YAT1_RHOBL. Based on the information provided herein, PRO1155 may play a role in providing neuroprotection and cognitive enhancement.

30 EXAMPLE 113: Isolation of cDNA clones Encoding Human PRO1156

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database, designated herein as 138851. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and

assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56261.

In light of an observed sequence homology between the DNA56261 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3675191, the Incyte EST clone 3675191 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 255 and is herein designated as DNA59853-1505.

The full length clone shown in Figure 255 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 212-214 and ending at the stop codon found at nucleotide positions 689-691 (Figure 255; SEQ ID NO:360). The predicted polypeptide precursor (Figure 256, SEQ ID NO:361) is 159 amino acids long. PRO1156 has a calculated molecular weight of approximately 17,476 daltons, an estimated pI of approximately 9.15, a signal peptide sequence at about amino acids 1 to about 22, and potential N-glycosylation sites at about amino acids 27-30 and 41-44.

Clone DNA59853-1505 was deposited with the ATCC on June 16, 1998 and is assigned ATCC deposit no. 209985.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence shown in Figure 256 (SEQ ID NO:361), revealed some homology between the PRO1156 amino acid sequence and the following Dayhoff sequences: D45027_1, P_R79914, JC5309, KBF2_HUMAN, AF010144_1, GEN14351, S68681, P_R79915, ZMTAC_3, and HUMCPGO_1.

20 EXAMPLE 114: Isolation of cDNA Clones Encoding Human PRO1098

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56377.

In light of an observed sequence homology between the DNA56377 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3050917, the Incyte EST clone 3050917 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 257 and is herein designated as DNA59854-1459.

The entire nucleotide sequence of DNA59854-1459 is shown in Figure 257 (SEQ ID NO:362). Clone DNA59854-1459 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon at nucleotide positions 292-294 of SEQ ID NO:362 (Figure 257). The predicted polypeptide precursor is 78 amino acids long (Figure 258). The full-length PRO1098 protein

shown in Figure 258 has an estimated molecular weight of about 8,396 daltons and a pl of about 7.66. Clone DNA59854-1459 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 258, a signal peptide appears to be at about amino acids 1-19 of SEQ ID NO:363, an N-glycosylation site appears to be at about amino acids 37-40 of SEQ ID NO:363, and N-myristoylation sites appear to be at about 15-20, 19-24 and 60-65 of SEQ ID NO:363.

EXAMPLE 115: Isolation of cDNA clones Encoding Human PRO1127

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57959.

In light of an observed sequence homology between the DNA57959 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 685126, the Merck EST clone 685126 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 259 and is herein designated as DNA60283-1484.

The full-length-clone shown in Figure 259 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 126-128 and ending at the stop codon found at nucleotide positions 327-329 (Figure 259; SEQ ID NO:364). The predicted polypeptide precursor (Figure 260, SEQ ID NO:365) is 67 amino acids long including a signal peptide at about 1-29 of SEQ ID NO:365. PRO1127 has a calculated molecular weight of approximately 7,528 daltons and an estimated pl of approximately 4.95. Clone DNA60283-1484 was deposited with the ATCC on July 1, 1998 and is assigned ATCC deposit no. 203043. It is understood that the deposited clone has the actual sequence, whereas representations which may have minor sequencing errors are presented herein.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 260 (SEQ ID NO:365), revealed some homology between the PRO1127 amino acid sequence and the following Dayhoff sequences: AF037218_48, P_W09638, HBA_HETPO, S39821, KR2_EBV, CET20D3_8, HCU37630_1, HS193B12_10, S40012 and TRITUBC 1.

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EXAMPLE 116: Isolation of cDNA clones Encoding Human PRO1126

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56250.

In light of an observed sequence homology between the DNA56250 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1437250, the Incyte EST clone 1437250 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 261 and is herein designated as DNA60615-1483.

Clone DNA60615-1483 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 110-112 and ending at the stop codon at nucleotide positions 1316-1318 (Figure 261). The predicted polypeptide precursor is 402 amino acids long (Figure 262). The full-length PRO1126 protein shown in Figure 262 has an estimated molecular weight of about 45,921 daltons and a pI of about 8.60. Analysis of the full-length PRO1126 sequence shown in Figure 262 (SEQ ID NO:367) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25 and potential N-glycosylation sites from about amino acid 66 to about amino acid 69, from about amino acid 138 to about amino acid 141 and from about amino acid 183 to about amino acid 186. Clone DNA60615-1483 has been deposited with ATCC on June 16, 1998 and is assigned ATCC deposit no. 209980.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 262 (SEQ ID NO:367), evidenced significant homology between the PRO1126 amino acid sequence and the following Dayhoff sequences: I73636, NOMR_HUMAN, MMUSMYOC3_1, HS454G6_1, P_R98225, RNU78105_1, RNU72487_1, AF035301_1, CEELC48E7_4 and CEF11C3_3.

EXAMPLE 117: Isolation of cDNA clones Encoding Human PRO1125

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence

obtained therefrom is herein designated DNA56540.

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In light of an observed sequence homology between the DNA56540 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1486114, the Incyte EST clone 1486114 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 263 and is herein designated as DNA60615-1483.

The full length clone shown in Figure 263 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 47-49 and ending at the stop codon found at nucleotide positions 1388-1390 (Figure 263; SEQ ID NO:368). The predicted polypeptide precursor (Figure 264, SEQ ID NO:369) is 447 amino acids long. PRO1125 has a calculated molecular weight of approximately 49,798 daltons and an estimated pI of approximately 9.78. Clone DNA60619-1482 has been deposited with ATCC and is assigned ATCC deposit no. 209993. It is understood that the clone has the actual sequence and that the sequences herein are representations based on current techniques which may be prone to minor errors.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1125 shows some sequence identity with the following Dayhoff designations: RCO1_NEUCR; S58306; PKWA_THECU; S76086; P_R85881; HET1_PODAN; SPU92792_1; APAF HUMAN; S76414 and S59317.

EXAMPLE 118: Isolation of cDNA clones Encoding Human PRO1186

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56748.

In light of an observed sequence homology between the DNA56748 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3476792, the Incyte EST clone 3476792 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 265 and is herein designated as DNA60621-1516.

The full length clone shown in Figure 265 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 91-93 and ending at the stop codon found at nucleotide positions 406-408 (Figure 265; SEQ ID NO:370). The predicted polypeptide precursor (Figure 266, SEQ ID NO:371) is 105 amino acids long. The signal peptide is at amino acids 1-19 of SEQ ID NO:371. PRO1186 has a calculated molecular weight of approximately 11,715 daltons and an estimated pI of approximately 9.05. Clone DNA60621-1516 was deposited with the ATCC on August 4, 1998 and is assigned ATCC deposit no. 203091.

PCT/US99/12252 WO 99/63088

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 266 (SEQ ID NO:371), revealed some sequence identity between the PRO1186 amino acid sequence and the following Dayhoff sequences: VPRA_DENPO, LFE4_CHICK, AF034208_1, AF030433_1, A55035, COL_RABIT, CELB0507_9, S67826_1, S34665 and CRU73817_1.

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EXAMPLE 119: Isolation of cDNA clones Encoding Human PRO1198

An initial DNA sequence referred to herein as DNA52083 was identified using a yeast screen in a human umbilical vein endothelial cell cDNA library that preferentially represents the 5' ends of the primary cDNA clones. DNA52083 was compared to ESTs from public databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA), using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. The ESTs were clustered and assembled into a consensus DNA sequence using the computer program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs was obtained from human breast skin tissue biopsy. This consensus sequence is designated herein as DNA52780.

In light of an observed sequence homology between the DNA52780 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3852910, the Incyte EST clone 3852910 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 267 and is herein designated as DNA60622-1525.

The full length DNA60622-1525 clone shown in Figure 267 (SEQ ID NO:372) contained a single open reading frame with an apparent translational initiation site at nucleotide positions 54 to 56 and ending at the stop codon found at nucleotide positions 741 to 743. The predicted polypeptide precursor, which is shown in Figure 268 (SEQ ID NO:373), is 229 amino acids long. PRO1198 has a calculated molecular weight of approximately 25,764 daltons and an estimated pI of approximately 9.17. There is a signal peptide sequence at about amino acids 1 through 34. There is sequence identity with glycosyl hydrolases family 31 protein at about amino acids 142 to about 175.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 268 (SEQ ID NO:373), revealed some homology between the PRO1198 amino acid sequence and the following Dayhoff sequences: ATF6H11_6, UCRI_RAT, TOBSUP2NT_1, RCUERF3_1, AMU88186_1, P_W22485, S56579, AF040711_1, DPP4_PIG.

30 deposit no. 203090.

Clone DNA60622-1525 was been deposited with the ATCC on August 4, 1998, and is assigned ATCC

EXAMPLE 120: Isolation of cDNA clones Encoding Human PRO1158

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single 35 EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The

homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., <u>Methods in Enzymology</u> 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57248.

In light of an observed sequence homology between the DNA57248 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2640776, the Incyte EST clone 2640776 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 269 and is herein designated as DNA60625-1507.

The full length clone shown in Figure 269 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 163 to 165 and ending at the stop codon found at nucleotide positions 532 to 534 (Figure 269; SEQ ID NO:374). The predicted polypeptide precursor (Figure 270, SEQ ID NO:375) is 123 amino acids long. PRO1158 has a calculated molecular weight of approximately 13,113 daltons and an estimated pI of approximately 8.53. Additional features include a signal peptide sequence at about amino acids 1-19, a transmembrane domain at about amino acids 56-80, and a potential N-glycosylation site at about amino acids 36-39. Clone DNA60625-1507 was deposited with the ATCC on June 16, 1998 and is assigned ATCC deposit no. 209975.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 270 (SEQ ID NO:375), revealed some homology between the PRO1158 amino acid sequence and the following Dayhoff sequences: ATAC00310510F18A8.10, P_R85151, PHS2_SOLTU, RNMHCIBAC_1, RNA1FMHC_1, I68771, RNRT1A10G_1, PTPA_HUMAN, HUMGACA 1, and CHKPTPA 1.

EXAMPLE 121: Isolation of cDNA clones Encoding Human PRO1159

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57221.

In light of an observed sequence homology between the DNA57221 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 376776, the Incyte EST clone 376776 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 271 and is herein designated as DNA60627-1508.

Clone DNA60627-1508 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 92-94 and ending at the stop codon at nucleotide positions 362-364 (Figure 271). The predicted polypeptide precursor is 90 amino acids long (Figure 272). The full-length PRO1159 protein shown in Figure 272 has an estimated molecular weight of about 9,840 daltons and a pI of about 10.13. Analysis of the full-length PRO1159 sequence shown in Figure 272 (SEQ ID NO:377) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15 and a potential N-glycosylation site from about amino acid 38 to about amino acid 41. Clone DNA60627-1508 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203092.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 272 (SEQ ID NO:377), evidenced significant homology between the PRO1159 amino acid sequence and the following Dayhoff sequences: AF016494_6, AF036708_20, DSSCUTE_1, D89100_1, S28060, MEFA_XENLA, AF020798_12, G70065, E64423, JQ2005.

EXAMPLE 122: Isolation of cDNA clones Encoding Human PRO1124

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single

EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of
expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary
EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The
homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., * Methods in
Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90)
or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with
the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence
obtained therefrom is herein designated DNA56035.

In light of an observed sequence homology between the DNA56035 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2767646, the Incyte EST clone 2767646 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 273 and is herein designated as DNA60629-1481.

The full length clone shown in Figure 273 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 25-27 and ending at the stop codon found at nucleotide positions 2782-2784 (Figure 273; SEQ ID NO:378). The predicted polypeptide precursor (Figure 274, SEQ ID NO:379) is 919 amino acids long. PRO1124 has a calculated molecular weight of approximately 101,282 daltons and an estimated pI of approximately 5.37. Clone DNA60629-1481 has been deposited with the ATCC and is assigned ATCC deposit no. 209979. It is understood that the deposited clone has the actual sequence, whereas only representations based on current sequencing techniques which may include normal and minor errors, are provided herein.

Based on a WU-BLAST2 sequence alignment analysis of the full-length sequence, PRO1124 shows significant amino acid sequence identity to a chloride channel protein and to ECAM-1. Specifically, the following Dayhoff designations were identified as having sequence identity with PRO1124: ECLC_BOVIN,

AF001261_1, P_W06548, SSC6A10_1, AF004355_1, S76691, AF017642, BYU06866_2, CSA_DICDI and SAU47139 2.

EXAMPLE 123: Isolation of cDNA clones Encoding Human PRO1287

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA)

was searched and an EST was identified which showed homology to the fringe protein. This EST sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence obtained is herein designated DNA40568.

Based on the DNA40568 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1287. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, supra, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTCGGGGAAAGGGACTTGATGTTGG-3' (SEQ ID NO:382)

reverse PCR primer 1 5'-GCGAAGGTGAGCCTCTATCTCGTGCC-3' (SEQ ID NO:383)

25 reverse PCR primer 2 5'-CAGCCTACACGTATTGAGG-3' (SEQ ID NO:384)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40568 sequence which had the following nucleotide sequence

hybridization probe

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5'-CAGTCAGTACAATCCTGGCATAATATACGGCCACCATGATGCAGTCCC-3' (SEQ ID NO:385).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO1287 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human bone marrow tissue. The cDNA libraries used to isolated the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD;

pRK5B is a precursor of pRK5D that does not contain the Sfil site; see, Holmes et al., <u>Science</u>, <u>253</u>:1278-1280 (1991)) in the unique Xhol and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1287 (designated herein as DNA61755-1554 [Figure 275, SEQ ID NO:380]) and the derived protein sequence for PRO1287.

The entire nucleotide sequence of DNA61755-1554 is shown in Figure 275 (SEQ ID NO:380). The full length clone contained a single open reading frame with an apparent translational initiation site at nucleotide positions 655-657 and a stop signal at nucleotide positions 2251-2253 (Figure 275, SEQ ID NO:380). The predicted polypeptide precursor is 532 amino acids long, has a calculated molecular weight of approximately 61,351 daltons and an estimated pI of approximately 8.77. Analysis of the full-length PRO1287 sequence shown in Figure 276 (SEQ ID NO:381) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 27 and potential N-glycosylation sites from about amino acid 315 to about amino acid 318 and from about amino acid 324 to about amino acid 327. Clone DNA61755-1554 has been deposited with ATCC on August 11, 1998 and is assigned ATCC deposit no. 203112.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 276 (SEQ ID NO:381), evidenced significant homology between the PRO1287 amino acid sequence and the following Dayhoff sequences: CET24D1_1, EZRI_BOVIN, GGU19889_1, CC3_YEAST, S74244, NALS_MOUSE, MOES_PIG, S28660, S44860 and YNA4_CAEEL.

20 EXAMPLE 124: Isolation of cDNA clones Encoding Human PRO1312

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DNA55773 was identified in a human fetal kidney cDNA library using a yeast screen that preferentially represents the 5' ends of the primary cDNA clones. Based on the DNA55773 sequence, oligonucleotides were synthesized for use as probes to isolate a clone of the full-length coding sequence for PRO1312.

The full length DNA61873-1574 clone shown in Figure 277 (SEQ ID NO:386) contained a single open reading frame with an apparent translational initiation site at nucleotide positions 7-9 and ending at the stop codon found at nucleotide positions 643-645. The predicted polypeptide precursor is 212 amino acids long (Figure 278, SEQ ID NO:387). PRO1312 has a calculated molecular weight of approximately 24,024 daltons and an estimated pI of approximately 6.26. Other features include a signal peptide at about amino acids 1-14; a transmembrane domain at about amino acids 141-160, and potential N-glycosylation sites at about amino acids 76-79 and 93-96.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 278 (SEQ ID NO:387), revealed some homology between the PRO1312 amino acid sequence and the following Dayhoff sequences: GCINTALPH_1, GIBMUC1A_1, P_R96298, AF001406_1, PVU88874_1, P_R85151, AF041409_1, CELC50F2_7, C45875, and AB009510 21.

Clone DNA61873-1574 has been deposited with ATCC and is assigned ATCC deposit no. 203132.

EXAMPLE 125: Isolation of cDNA clones Encoding Human PRO1192

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein DNA35924. Based on the DNA35924 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1192.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-CCGAGGCCATCTAGAGGCCAGAGC-3' (SEQ ID NO:390)

reverse PCR primer: 5'-ACAGGCAGAGCCAATGGCCAGAGC-3' (SEQ ID NO:391).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus 10 DNA35924 sequence which had the following nucleotide sequence:

hybridization probe:

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5'-GAGAGGACTGCGGGAGTTTGGGACCTTTGTGCAGACGTGCTCATG-3' (SEQ ID NO:392).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1192 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver and spleen tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1192 designated herein as DNA62814-1521 and shown in Figure 279 (SEQ ID NO:388); and the derived protein sequence for PRO1192 which is shown in Figure 280 (SEQ ID NO:389).

The entire coding sequence of PRO1192 is shown in Figure 279 (SEQ ID NO:388). Clone DNA62814-1521 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and an apparent stop codon at nucleotide positions 766-768. The predicted polypeptide precursor is 215 amino acids long. The predicted polypeptide precursor has the following features: a signal peptide at about amino acids 1-21; a transmembrane domain at about amino acids 153-176; potential N-glycosylation sites at about amino acids 39-42 and 118-121; and homology with myelin P0 proteins at about amino acids 27-68 and 99-128 of Figure 280. The full-length PRO1192 protein shown in Figure 280 has an estimated molecular weight of about 24,484 daltons and a pl of about 6.98.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 280 (SEQ ID NO:389), revealed homology between the PRO1192 amino acid sequence and the following Dayhoff sequences: GEN12838, MYPO_HUMAN, AFO49498_1, GEN14531, P_W14146, HS46KDA_1, CINB_RAT, OX2G_RAT, D87018_1, and D86996_2.

Clone DNA62814-1521 was deposited with the ATCC on August 4, 1998, and is assigned ATCC deposit no. 203093.

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EXAMPLE 126: Isolation of cDNA clones Encoding Human PRO1160

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above This consensus sequence is herein designated DNA40650. Based on the DNA40650 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1160.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GCTCCCTGATCTTCATGTCACCACC-3' (SEQ ID NO:395)

reverse PCR primer 5'-CAGGGACACACTCTACCATTCGGGAG-3' (SEQ ID NO:396)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40650 sequence which had the following nucleotide sequence

hybridization probe

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5'-CCATCTTTCTGGTCTCTGCCCAGAATCCGACAACAGCTGCTC-3' (SEQ ID NO:397)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1160 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1160 (designated herein as DNA62872-1509 [Figure 281, SEQ ID NO: 393]) and the derived protein sequence for PRO1160.

The entire nucleotide sequence of DNA62872-1509 is shown in Figure 281 (SEQ ID NO:393). Clone DNA62872-1509 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 40-42 and ending at the stop codon at nucleotide positions 310-312 (Figure 281). The predicted polypeptide precursor is 90 amino acids long (Figure 282). The full-length PRO1160 protein shown in Figure 282 has an estimated molecular weight of about 9,039 daltons and a pl of about 4.37. Analysis of the full-length PRO1160 sequence shown in Figure 282 (SEQ ID NO:394) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19 and a protein kinase C phosphorylation site from about amino acid 68 to about amino acid 70. Clone DNA62872-1509 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203100.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 282 (SEQ ID NO:394), evidenced significant homology between the PRO1160 amino acid sequence and the following Dayhoff sequences: B30305, GEN13490, I53641, S53363, HA34_BRELC, SP96_DICDI, S36326, SSU51197_10, MUC1_XENLA, TCU32448_1 and AF000409_1.

35 EXAMPLE 127: Isolation of cDNA clones Encoding Human PRO1187

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of

expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57726.

In light of an observed sequence homology between the DNA57726 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 358563, the Incyte EST clone 358563 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 283 and is herein designated as DNA62876-1517.

The full length clone shown in Figure 283 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and ending at the stop codon found at nucleotide positions 481-483 (Figure 283; SEQ ID NO:398). The predicted polypeptide precursor (Figure 284, SEQ ID NO:399) is 120 amino acids long. The signal peptide is at about amino acids 1-17 of SEQ ID NO:399.

PRO1187 has a calculated molecular weight of approximately 12,925 daltons and an estimated pl of approximately 9.46. Clone DNA62876-1517 was deposited with the ATCC on August 4, 1998 and is assigned ATCC deposit no. 203095. It is understood that the deposited clone contains the actual sequence and that the representations herein may have minor sequencing errors.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 284 (SEQ ID NO:399), revealed some sequence identity (and therefore some relation) between the PRO1187 amino acid sequence and the following Dayhoff sequences:—MGNENDOBX_1,—CELF41G3_9,—AMPG_STRLI,—HSBBOVHERL_2,—LEEXTEN10_1,—AF029958_1 and P_W04957.

25 EXAMPLE 128: Isolation of cDNA clones Encoding Human PRO1185

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56426.

In light of an observed sequence homology between the DNA56426 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3284411, the Incyte EST clone 3284411 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

The sequence of this cDNA insert is shown in Figure 285 and is herein designated as DNA62881-1515.

The full length DNA62881-1515 clone shown in Figure 285 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 4-6 and ending at the stop codon found at nucleotide positions 598-600 (Figure 285; SEQ ID NO:400). The predicted polypeptide precursor (Figure 286, SEQ ID NO:401) is 198 amino acids long. The signal peptide is at about amino acids 1-21 of SEQ ID NO:401. PRO1185 has a calculated molecular weight of approximately 22,105 daltons and an estimated pI of approximately 7.73. Clone DNA62881-1515 has been deposited with the ATCC and is assigned ATCC deposit no. 203096.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 286 (SEQ ID NO:401), revealed some sequence identity between the PRO1185 amino acid sequence and the following Dayhoff sequences: TUP1_YEAST, AF041382_1, MAOM_SOLTU, SPPBPHU9_1,I41024, EPCPLCFAIL_1, HSPLEC_1, YKL4_CAEEL, A44643, TGU65922_1.

EXAMPLE 129: Isolation of cDNA clones Encoding Human PRO1345

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA47364. Based on the DNA47364 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1345.

20 PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCTGGTTATCCCCAGGAACTCCGAC-3' (SEQ ID NO:404)

reverse PCR primer 5'-CTCTTGCTGCTGCGACAGGCCTC-3' (SEQ ID NO:405)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47364 sequence which had the following nucleotide sequence

25 <u>hybridization probe</u>

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5'-CGCCCTCCAAGACTATGGTAAAAGGAGCCTGCCAGGTGTCAATGAC-3' (SEQ ID NO:406)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1345 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast carcinoma tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1345 (designated herein as DNA64852-1589 [Figure 287, SEQ ID NO:402]) and the derived protein sequence for PRO1345.

The entire nucleotide sequence of DNA64852-1589 is shown in Figure 287 (SEQ ID NO:402). Clone

DNA64852-1589 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 7-9 or 34-36 and ending at the stop codon at nucleotide positions 625-627 (Figure 287). The predicted polypeptide precursor is 206 amino acids long (Figure 288). The full-length PRO1345 protein shown in Figure

288 has an estimated molecular weight of about 23,190 daltons and a pl of about 9.40. Analysis of the full-length PRO1345 sequence shown in Figure 288 (SEQ ID NO:403) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31 or from about amino acid 10 to about amino acid 31 and a C-type lectin domain signature sequence from about amino acid 176 to about amino acid 190. Clone DNA64852-1589 has been deposited with ATCC on August 18, 1998 and is assigned ATCC deposit no. 203127.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 288 (SEQ ID NO:403), evidenced significant homology between the PRO1345 amino acid sequence and the following Dayhoff sequences: BTU22298_1, TETN_CARSP, TETN_HUMAN, MABA_RAT, S34198, P_W13144, MACMBPA_1, A46274, PSPD_RAT AND P R32188.

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EXAMPLE 130: Isolation of cDNA clones Encoding Human PRO1245

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56019.

In light of an observed sequence homology between the DNA56019 consensus sequence and an EST sequence encompassed within the Incyte EST clone no.-1327836, the Incyte EST clone-1327836 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 289 and is herein designated as DNA64884-1527.

The full length clone shown in Figure 289 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 79-81 and ending at the stop codon found at nucleotide positions 391-393 (Figure 289; SEQ ID NO:407). The predicted polypeptide precursor (Figure 290, SEQ ID NO:408) is 104 amino acids long, with a signal peptide sequence at about amino acid 1 to about amino acid 18. PRO1245 has a calculated molecular weight of approximately 10,100 daltons and an estimated pI of approximately 8.76.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 290 (SEQ ID NO:408), revealed some homology between the PRO1245 amino acid sequence and the following Dayhoff sequences: SYA_THETH, GEN11167, MTV044_4, AB011151_1, RLAJ2750_3, SNELIPTRA_1, S63624, C28391, A37907, and S14064.

Clone DNA64884-1245 was deposited with the ATCC on August 25, 1998 and is assigned ATCC deposit no. 203155.

EXAMPLE 131: Isolation of cDNA clones Encoding Human PRO1358

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 88718, the Incyte EST clone 88718 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 291 and is herein designated as DNA64890-1612.

The full length clone shown in Figure 291 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 86 through 88 and ending at the stop codon found at nucleotide positions 1418 through 1420 (Figure 291; SEQ ID NO:409). The predicted polypeptide precursor (Figure 292, SEQ ID NO:410) is 444 amino acids long. The signal peptide is at about amino acids 1-18 of SEQ ID NO:410. PRO1358 has a calculated molecular weight of approximately 50,719 daltons and an estimated pl of approximately 8.82. Clone DNA64890-1612 was deposited with the ATCC on August 18, 1998 and is assigned ATCC deposit no. 203131.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 292 (SEQ ID NO:410), revealed sequence identity between the PRO1358 amino acid sequence and the following Dayhoff sequences: P_W07607, AB000545_1, AB000546_1, A1AT_RAT, AB015164_1, P_P50021, COTR_CAVPO, and HAMHPP_1. The variants claimed in this application exclude these sequences.

EXAMPLE 132: Isolation of cDNA clones Encoding Human PRO1195

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55716.

In light of an observed sequence homology between the DNA55716 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3252980, the Incyte EST clone 3252980 was purchased

and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 293 and is herein designated as DNA65412-1523.

The full length clone shown in Figure 293 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon found at nucleotide positions 511-513 (Figure 293; SEQ ID NO:411). The predicted polypeptide precursor (Figure 294, SEQ ID NO:412) is 151 amino acids long. The signal sequence is at about amino acids 1-22 of SEQ ID NO:412. PRO1195 has a calculated molecular weight of approximately 17,277 daltons and an estimated pI of approximately 5.33. Clone DNA65412-1523 was deposited with the ATCC on August 4, 1998 and is assigned ATCC deposit no. 203094.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 294 (SEQ ID NO:412), revealed some sequence identity between the PRO1195 amino acid sequence and the following Dayhoff sequences: MMU28486_1, AF044205_1, P_W31186, CELK03C7_1, F69034, EF1A_METVA, AF024540_1, SSU90353_1, MRSP_STAAU and P_R97680.

EXAMPLE 133: Isolation of cDNA clones Encoding Human PRO1270

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57951.

In light of an observed sequence homology between the DNA57951 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 124878, the Merck EST clone 124878 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 295 and is herein designated as DNA66308-1537.

Clone DNA66308-1537 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 103-105 and ending at the stop codon at nucleotide positions 1042-1044 (Figure 295). The predicted polypeptide precursor is 313 amino acids long (Figure 296). The full-length PRO1270 protein shown in Figure 296 has an estimated molecular weight of about 34,978 daltons and a pI of about 5.71. Analysis of the full-length PRO1270 sequence shown in Figure 296 (SEQ ID NO:414) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 16, a potential N-glycosylation site from about amino acid 163 to about amino acid 166 and glycosaminoglycan attachment sites from about amino acid 74 to about amino acid 77 and from about amino acid 289 to about amino acid 292. Clone DNA66308-1537 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203159.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 296 (SEQ ID NO:414), evidenced significant homology between the PRO1270 amino acid sequence and the following Dayhoff sequences: XLU86699_1, S49589, FIBA_PARPA, FIBB_HUMAN, P_R47189, AF004326_1, DRTENASCN_1, AF004327_1, P_W01411 and FIBG BOVIN.

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EXAMPLE 134: Isolation of cDNA clones Encoding Human PRO1271

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuricals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57955.

In light of an observed sequence homology between the DNA57955 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA625350, the Merck EST clone AA625350 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 297 and is herein designated as DNA66309-1538.

Clone DNA66309-1538 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 94-96 and ending at the stop codon at nucleotide positions 718-720 (Figure 297). The predicted polypeptide precursor is 208 amino acids long (Figure 298). The full-length PRO1271 protein shown in Figure 298 has an estimated molecular weight of about 21,531 daltons and a pl of about 8.99. Analysis of the full-length PRO1271 sequence shown in Figure 298 (SEQ ID NO:416) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31 and a transmembrane domain from about amino acid 166 to about amino acid 187. Clone DNA66309-1538 has been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no. 203235.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 298 (SEQ ID NO:416), evidenced significant homology between the PRO1271 amino acid sequence and the following Dayhoff sequences: S57180, S63257, AGA1_YEAST, BPU43599_1, YS8A_CAEEL, S67570, LSU54556_2, S70305, VGLX_HSVEB, and D88733 1.

EXAMPLE 135: Isolation of cDNA clones Encoding Human PRO1375

A Merck/Wash. U. database was searched and a Merck EST was identified. This sequence was then put in a program which aligns it with other seequences from the Swiss-Prot public database, public EST databases (e.g., GenBank, Merck/Wash. U.), and a proprietary EST database (LIFESEQ®, Incyte

Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)] as a comparison of the extracellular domain (ECD) protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

A consensus DNA sequence was assembled relative to other EST sequences using phrap. This consensus sequence is designated herein "DNA67003".

Based on the DNA 67003 consensus sequence, the nucleic acid (SEQ ID NO:417) was identified in a human pancreas library. DNA sequencing of the clone gave the full-length DNA sequence for PRO1375 and the derived protein sequence for PRO1375.

The entire coding sequence of PRO1375 is shown in Figure 299 (SEQ ID NO:417). Clone DNA67004-1614 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 104-106 and an apparent stop codon at nucleotide positions 698-700 of SEQ ID NO:417. The predicted polypeptide precursor is 198 amino acids long. The transmembrane domains are at about amino acids 11-28 (type II) and 103-125 of SEQ ID NO:418. Clone DNA67004-1614 has been deposited with ATCC and is assigned ATCC deposit no. 203115. The full-length PRO1375 protein shown in Figure 300 has an estimated molecular weight of about 22,531 daltons and a pl of about 8.47.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 300 (SEQ ID NO:418), revealed sequence identity between the PRO1375 amino acid sequence and the following Dayhoff sequences: AF026198_5, CELR12C12_5, S73465, Y011_MYCPN, S64538_1, P_P8150, MUVSHPO10_1, VSH_MUMPL and CVU59751_5.

EXAMPLE 136: Isolation of cDNA clones Encoding Human PRO1385

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57952.

In light of an observed sequence homology between the DNA57952 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3129630, the Incyte EST clone 3129630 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 301 and is herein designated as DNA68869-1610.

Clone DNA68869-1610 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 26-28 and ending at the stop codon at nucleotide positions 410-412 (Figure 301). The predicted polypeptide precursor is 128 amino acids long (Figure 302). The full-length PRO1385 protein shown in Figure 302 has an estimated molecular weight of about 13,663 daltons and a pl of about 10.97. Analysis of the full-length PRO1385 sequence shown in Figure 302 (SEQ ID NO:420) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, and glycosylaminoglycan attachment sites from about amino acid 82 to about amino acid 85 and from about amino acid 91 to about amino acid 94. Clone DNA68869-1610 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203164.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 302 (SEQ ID NO:420), evidenced low homology between the PRO1385 amino acid sequence and the following Dayhoff sequences: CELT14A8_1, LMNACHRA1_1, HXD9_HUMAN, CHKCMLF_1, HS5PP34_2, DMDRING_1, A37107_1, MMLUNGENE_1, PUM_DROME and DMU25117_1.

15 EXAMPLE 137: Isolation of cDNA clones Encoding Human PRO1387

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Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56259.

In light of an observed sequence homology between the DNA56259 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3507924, the Incyte EST clone 3507924 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 303 and is herein designated as DNA68872-1620.

Clone DNA68872-1620 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 85-87 and ending at the stop codon at nucleotide positions 1267-1269 (Figure 303). The predicted polypeptide precursor is 394 amino acids long (Figure 304). The full-length PRO1387 protein shown in Figure 304 has an estimated molecular weight of about 44,339 daltons and a pI of about 7.10. Analysis of the full-length PRO1387 sequence shown in Figure 304 (SEQ ID NO:422) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19, a transmembrane domain from about amino acid 275 to about amino acid 296, potential N-glycosylation sites from about amino acid 76 to about amino acid 79, from about amino acid 231 to about amino acid 234, from about amino acid 302 to about amino acid 305, from about amino acid 307 to about amino acid 310 and from about amino acid 376 to about amino acid 305, from about amino acid 307 to about amino acid 310 and from about amino acid 376 to about amino acid

379, and amino acid sequence blocks having homology to myelin p0 protein from about amino acid 210 to about amino acid 239 and from about amino acid 92 to about amino acid 121. Clone DNA68872-1620 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203160.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 304 (SEQ ID NO:422), evidenced significant homology between the PRO1387 amino acid sequence and the following Dayhoff sequences: P_W36955, MYPO_HETFR, HS46KDA_1, AF049498_1, MYOO_HUMAN, AF030454_1, A53268, SHPTCRA_1, P W14146 and GEN12838.

EXAMPLE 138: Isolation of cDNA clones Encoding Human PRO1384

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA54192. Based on the DNA54192 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1384.

PCR primers (forward and reverse) were synthesized:

5 forward PCR primer 5'-TGCAGCCCCTGTGACACAAACTGG-3' (SEQ ID NO:425)
reverse PCR primer 5'-CTGAGATAACCGAGCCATCCTCCCAC-3' (SEQ ID NO:426)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA54192 sequence which had the following nucleotide sequence:

hybridization probe

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20 5'-GGAGATAGCTGCTATGGGTTCTTCAGGCACAACTTAACATGGGAAG-3' (SEQ ID NO:427)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1384 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1384 (designated herein as DNA71159-1617 [Figure 305, SEQ ID NO:423]; and the derived protein sequence for PRO1384.

The entire coding sequence of PRO1384 is shown in Figure 305 (SEQ ID NO:423). Clone DNA71159-1617 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 182-184 and an apparent stop codon at nucleotide positions 869-871. The predicted polypeptide precursor is 229 amino acids long. The full-length PRO1384 protein shown in Figure 306 has an estimated molecular weight of about 26,650 daltons and a pI of about 8.76. Additional features include a type II transmembrane domain at about amino acids 32-57, and potential N-glycosylation sites at about amino acids 68-71, 120-123, and 134-137.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 306 (SEQ ID NO:424), revealed homology between the PRO1384 amino acid sequence and the following Dayhoff sequences: AF054819_1, HSAJ1687_1, AF009511_1,AB010710_1,GEN13595,HSAJ673_1,GEN13961,AB005900_1,LECH_CHICK,AF021349_1,

and NK13_RAT.

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Clone DNA71159-1617 has been deposited with ATCC and is assigned ATCC deposit no. 203135.

EXAMPLE 139: Use of PRO as a hybridization probe

The following method describes use of a nucleotide sequence encoding PRO as a hybridization probe.

DNA comprising the coding sequence of full-length or mature PRO as disclosed herein is employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of PRO) in human tissue cDNA libraries or human tissue genomic libraries.

Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled PRO-derived probe to the filters is performed in a solution of 50% formamide, 5x SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2x Denhardt's solution, and 10% dextran sulfate at 42°C for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% SDS at 42°C.

DNAs having a desired sequence identity with the DNA encoding full-length native sequence PRO can then be identified using standard techniques known in the art.

EXAMPLE 140: Expression of PRO in E. coli

This example illustrates preparation of an unglycosylated form of PRO by recombinant expression in E. coli.

The DNA sequence encoding PRO is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector. A variety of expression vectors may be employed. An example of a suitable vector is pBR322 (derived from E. coli; see Bolivar et al., Gene, 2:95 (1977)) which contains genes for amplicilin and tetracycline resistance. The vector is digested with restriction enzyme and dephosphorylated. The PCR amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode for an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons, polyhis sequence, and enterokinase cleavage site), the PRO coding region, lambda transcriptional terminator, and an argU gene.

The ligation mixture is then used to transform a selected *E. coli* strain using the methods described in Sambrook et al., <u>supra</u>. Transformants are identified by their ability to grow on LB plates and antibiotic resistant colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA sequencing.

Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with antibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the solubilized PRO protein can then be purified using a metal chelating column under conditions that allow tight binding of the

protein.

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PRO may be expressed in *E. coli* in a poly-His tagged form, using the following procedure. The DNA encoding PRO is initially amplified using selected PCR primers. The primers will contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector, and other useful sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences are then ligated into an expression vector, which is used to transform an *E. coli* host based on strain 52 (W3110 fuhA(tonA) lon galE rpoHts(htpRts) clpP(lacIq). Transformants are first grown in LB containing 50 mg/ml carbenicillin at 30°C with shaking until an O.D.600 of 3-5 is reached. Cultures are then diluted 50-100 fold into CRAP media (prepared by mixing 3.57 g (NH₄)₂SO₄, 0.71 g sodium citrate 2H2O, 1.07 g KCl, 5.36 g Difco yeast extract, 5.36 g Sheffield hycase SF in 500 mL water, as well as 110 mM MPOS, pH 7.3, 0.55% (w/v) glucose and 7 mM MgSO₄) and grown for approximately 20-30 hours at 30°C with shaking. Samples are removed to verify expression by SDS-PAGE analysis, and the bulk culture is centrifuged to pellet the cells. Cell pellets are frozen until purification and refolding.

E. coli paste from 0.5 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution is stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution is centrifuged at 40,000 rpm in a Beckman Ultracentifuge for 30 min. The supernatant is diluted with 3-5 volumes of metal chelate column buffer (6 M guanidine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. The clarified extract is loaded onto a 5 ml Qiagen Ni-NTA metal chelate column equilibrated in the metal chelate column buffer. The column is washed with additional buffer containing 50 mM imidazole (Calbiochem, Utrol grade), pH 7.4. The protein is eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein are pooled and stored at 4°C. Protein concentration is estimated by its absorbance at 280 nm using the calculated extinction coefficient based on its amino acid sequence.

The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes are chosen so that the final protein concentration is between 50 to 100 micrograms/ml. The refolding solution is stirred gently at 4°C for 12-36 hours. The refolding reaction is quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the solution is filtered through a 0.22 micron filter and acetonitrile is added to 2-10% final concentration. The refolded protein is chromatographed on a Poros R1/H reversed phase column using a mobile buffer of 0.1% TFA with elution with a gradient of acetonitrile from 10 to 80%. Aliquots of fractions with A280 absorbance are analyzed on SDS polyacrylamide gels and fractions containing homogeneous refolded protein are pooled. Generally, the properly refolded species of most proteins are eluted at the lowest concentrations of acetonitrile since those species are the most compact with their hydrophobic interiors shielded from interaction with the reversed phase resin. Aggregated species are usually eluted at higher acetonitrile concentrations. In addition to resolving misfolded forms of proteins from the desired form, the reversed phase step also removes endotoxin

PCT/US99/12252 WO 99/63088

from the samples.

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Fractions containing the desired folded PRO polypeptide are pooled and the acetonitrile removed using a gentle stream of nitrogen directed at the solution. Proteins are formulated into 20 mM Hepes, pH 6.8 with 0.14 M sodium chloride and 4% mannitol by dialysis or by gel filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer and sterile filtered.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 141: Expression of PRO in mammalian cells

This example illustrates preparation of a potentially glycosylated form of PRO by recombinant expression in mammalian cells.

The vector, pRK5 (see EP 307,247, published March 15, 1989), is employed as the expression vector. Optionally, the PRO DNA is ligated into pRK5 with selected restriction enzymes to allow insertion of the PRO DNA using ligation methods such as described in Sambrook et al., supra. The resulting vector is called pRK5-PRO.

In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10 μg pRK5-PRO DNA is mixed with about 1 μg DNA encoding the VA RNA gene [Thimmappaya et al., Cell, 31:543 (1982)] and dissolved in 500 μ l of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M CaCl₂. To this mixture is added, dropwise, 500 μl of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM NaPO₄, and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200 μCi/ml ³⁵S-cysteine and 200 μCi/ml ³⁵S-methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS gel. The processed gel may be dried and exposed to film for a selected period of time to reveal the presence of PRO polypeptide. The cultures containing transfected cells may undergo further incubation (in serum free medium) and the medium is tested in selected bioassays.

In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulfate method described by Somparyrac et al., Proc. Natl. Acad. Sci., 12:7575 (1981). 293 cells are grown to maximal density in a spinner flask and 700 μ g pRK5-PRO DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5 µg/ml bovine insulin and $0.1 \,\mu g/ml$ bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed PRO can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

In another embodiment, PRO can be expressed in CHO cells. The pRK5-PRO can be transfected into CHO cells using known reagents such as CaPO₄ or DEAE-dextran. As described above, the cell cultures can be incubated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such as ³⁵S-methionine. After determining the presence of PRO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incubated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed PRO can then be concentrated and purified by any selected method.

Epitope-tagged PRO may also be expressed in host CHO cells. The PRO may be subcloned out of the pRK5 vector. The subclone insert can undergo PCR to fuse in frame with a selected epitope tag such as a polyhis tag into a Baculovirus expression vector. The poly-his tagged PRO insert can then be subcloned into a SV40 driven vector containing a selection marker such as DHFR for selection of stable clones. Finally, the CHO cells can be transfected (as described above) with the SV40 driven vector. Labeling may be performed, as described above, to verify expression. The culture medium containing the expressed poly-His tagged PRO can then be concentrated and purified by any selected method, such as by Ni²⁺-chelate affinity chromatography.

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PRO may also be expressed in CHO and/or COS cells by a transient expression procedure or in CHO cells by another stable expression procedure.

Stable expression in CHO cells is performed using the following procedure. The proteins are expressed as an IgG construct (immunoadhesin), in which the coding sequences for the soluble forms (e.g. extracellular domains) of the respective proteins are fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

Following PCR amplification, the respective DNAs are subcloned in a CHO expression vector using standard techniques as described in Ausubel et al., <u>Current Protocols of Molecular Biology</u>, Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., <u>Nucl. Acids Res.</u> 24:9 (1774-1779 (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductase (DHFR). DHFR expression permits selection for stable maintenance of the plasmid following transfection.

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect® (Quiagen), Dosper® or Fugene® (Boehringer Mannheim). The cells are grown as described in Lucas et al., <u>supra</u>. Approximately 3 x 10⁻⁷ cells are frozen in an ampule for further growth and production as described below.

The ampules containing the plasmid DNA are thawed by placement into water bath and mixed by vortexing. The contents are pipetted into a centrifuge tube containing 10 mLs of media and centrifuged at 1000 rpm for 5 minutes. The supernatant is aspirated and the cells are resuspended in 10 mL of selective media (0.2 μ m filtered PS20 with 5% 0.2 μ m diafiltered fetal bovine serum). The cells are then aliquoted into a 100 mL spinner containing 90 mL of selective media. After 1-2 days, the cells are transferred into a 250 mL spinner filled with 150 mL selective growth medium and incubated at 37%. After another 2-3 days, 250 mL, 500 mL and 2000 mL spinners are seeded with 3 x 10 $^{\circ}$ cells/mL. The cell media is exchanged with fresh media by

centrifugation and resuspension in production medium. Although any suitable CHO media may be employed, a production medium described in U.S. Patent No. 5,122,469, issued June 16, 1992 may actually be used. A 3L production spinner is seeded at 1.2×10^6 cells/mL. On day 0, the cell number pH ie determined. On day 1, the spinner is sampled and sparging with filtered air is commenced. On day 2, the spinner is sampled, the temperature shifted to 33°C, and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35% polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion) taken. Throughout the production, the pH is adjusted as necessary to keep it at around 7.2. After 10 days, or until the viability dropped below 70%, the cell culture is harvested by centrifugation and filtering through a 0.22 μ m filter. The filtrate was either stored at 4°C or immediately loaded onto columns for purification.

For the poly-His tagged constructs, the proteins are purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 ml/min. at 4°C. After loading, the column is washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein is subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 ml G25 Superfine (Pharmacia) column and stored at -80°C.

Immunoadhesin (Fc-containing) constructs are purified from the conditioned media as follows. The conditioned medium is pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 ml fractions into tubes containing 275 μ L of 1 M Tris buffer, pH 9. The highly purified protein is subsequently desalted into storage buffer as described above for the poly-His tagged proteins. The homogeneity is assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

25 EXAMPLE 142: Expression of PRO in Yeast

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The following method describes recombinant expression of PRO in yeast.

First, yeast expression vectors are constructed for intracellular production or secretion of PRO from the ADH2/GAPDH promoter. DNA encoding PRO and the promoter is inserted into suitable restriction enzyme sites in the selected plasmid to direct intracellular expression of PRO. For secretion, DNA encoding PRO can be cloned into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, a native PRO signal peptide or other mammalian signal peptide, or, for example, a yeast alpha-factor or invertase secretory signal/leader sequence, and linker sequences (if needed) for expression of PRO.

Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in selected fermentation media. The transformed yeast supernatants can be analyzed by precipitation with 10% trichloroacetic acid and separation by SDS-PAGE, followed by staining of the gels with Coomassie Blue stain.

Recombinant PRO can subsequently be isolated and purified by removing the yeast cells from the fermentation medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate containing PRO may further be purified using selected column chromatography resins.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

5 EXAMPLE 143: Expression of PRO in Baculovirus-Infected Insect Cells

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The following method describes recombinant expression of PRO in Baculovirus-infected insect cells.

The sequence coding for PRO is fused upstream of an epitope tag contained within a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the sequence encoding PRO or the desired portion of the coding sequence of PRO such as the sequence encoding the extracellular domain of a transmembrane protein or the sequence encoding the mature protein if the protein is extracellular is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme sites. The product is then digested with those selected restriction enzymes and subcloned into the expression vector.

Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGold™ virus DNA (Pharmingen) into Spodoptera frugiperda ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4 - 5 days of incubation at 28°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilley et al., Baculovirus expression vectors: A Laboratory Manual, Oxford: Oxford University Press (1994).

Expressed poly-his tagged PRO can then be purified, for example, by Ni²⁺-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., Nature, 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM MgCl₂; 0.1 mM EDTA; 10% glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% glycerol, pH 7.8) and filtered through a 0.45 µm filter. A Ni²⁺-NTA agarose column (commercially available from Qiagen) is prepared with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A₂₈₀ with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM phosphate; 300 mM NaCl, 10% glycerol, pH 6.0), which elutes nonspecifically bound protein. After reaching A₂₈₀ baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or Western blot with Ni²⁺-NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His₁₀-tagged PRO are pooled and dialyzed against loading buffer.

Alternatively, purification of the IgG tagged (or Fc tagged) PRO can be performed using known chromatography techniques, including for instance, Protein A or protein G column chromatography.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 144: Preparation of Antibodies that Bind PRO

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This example illustrates preparation of monoclonal antibodies which can specifically bind PRO.

Techniques for producing the monoclonal antibodies are known in the art and are described, for instance, in Goding, <u>supra</u>. Immunogens that may be employed include purified PRO, fusion proteins containing PRO, and cells expressing recombinant PRO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

Mice, such as Balb/c, are immunized with the PRO immunogen emulsified in complete Freund's adjuvant and injected subcutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, MT) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emulsified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically obtained from the mice by retro-orbital bleeding for testing in ELISA assays to detect anti-PRO antibodies.

After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

The hybridoma cells will be screened in an ELISA for reactivity against PRO. Determination of "positive" hybridoma cells secreting the desired monoclonal antibodies against PRO is within the skill in the art.

The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce ascites containing the anti-PRO monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion chromatography. Alternatively, affinity chromatography based upon binding of antibody to protein A or protein G can be employed.

EXAMPLE 145: Purification of PRO Polypeptides Using Specific Antibodies

Native or recombinant PRO polypeptides may be purified by a variety of standard techniques in the art of protein purification. For example, pro-PRO polypeptide, mature PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the PRO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-PRO polypeptide antibody to an activated chromatographic resin.

Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscataway, N.J.).

Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CnBr-activated SEPHAROSETM (Pharmacia LKB Biotechnology). The antibody

is coupled to the resin, the resin is blocked, and the derivative resin is washed according to the manufacturer's instructions.

Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction from cells containing PRO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the addition of detergent or by other methods well known in the art. Alternatively, soluble PRO polypeptide containing a signal sequence may be secreted in useful quantity into the medium in which the cells are grown.

A soluble PRO polypeptide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of PRO polypeptide (e.g., high ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt antibody/PRO polypeptide binding (e.g., a low pH buffer such as approximately pH 2-3, or a high concentration of a chaotrope such as urea or thiocyanate ion), and PRO polypeptide is collected.

EXAMPLE 146: Drug Screening

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This invention is particularly useful for screening compounds by using PRO polypeptides or binding fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the PRO polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between PRO polypeptide or a fragment and the agent being tested. Alternatively, one can examine the diminution in complex formation between the PRO polypeptide and its target cell or target receptors caused by the agent being tested.

Thus, the present invention provides methods of screening for drugs or any other agents which can affect a PRO polypeptide-associated disease or disorder. These methods comprise contacting such an agent with an PRO polypeptide or fragment thereof and assaying (I) for the presence of a complex between the agent and the PRO polypeptide or fragment, or (ii) for the presence of a complex between the PRO polypeptide or fragment and the cell, by methods well known in the art. In such competitive binding assays, the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO polypeptide or fragment is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular agent to bind to PRO polypeptide or to interfere with the PRO polypeptide/cell complex.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to a polypeptide and is described in detail in WO 84/03564, published on September 13, 1984. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art. Purified PRO polypeptide can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the

PCT/US99/12252 WO 99/63088

solid support.

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This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding PRO polypeptide specifically compete with a test compound for binding to PRO polypeptide or fragments thereof. In this manner, the antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with PRO polypeptide.

EXAMPLE 147: Rational Drug Design

The goal of rational drug design is to produce structural analogs of biologically active polypeptide of interest (i.e., a PRO polypeptide) or of small molecules with which they interact, e.g., agonists, antagonists, or inhibitors. Any of these examples can be used to fashion drugs which are more active or stable forms of the PRO polypeptide or which enhance or interfere with the function of the PRO polypeptide in vivo (c.f., Hodgson, Bio/Technology, 2: 19-21 (1991)).

In one approach, the three-dimensional structure of the PRO polypeptide, or of an PRO polypeptide-inhibitor complex, is determined by x-ray crystallography, by computer modeling or, most typically, by a combination of the two approaches. Both the shape and charges of the PRO polypeptide must be ascertained to elucidate the structure and to determine active site(s) of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be gained by modeling based on the structure of homologous proteins. In both cases, relevant structural information is used to design analogous PRO polypeptide-like molecules or to identify efficient inhibitors. Useful examples of rational drug design may include molecules which have improved activity or stability as shown by Braxton and Wells, Biochemistry, 31:7796-7801 (1992) or which act as inhibitors, agonists, or antagonists of native peptides as shown by Athauda et al., J. Biochem., 113:742-746 20 (1993).

It is also possible to isolate a target-specific antibody, selected by functional assay, as described above, and then to solve its crystal structure. This approach, in principle, yields a pharmacore upon which subsequent drug design can be based. It is possible to bypass protein crystallography altogether by generating anti-idiotypic antibodies (anti-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image, the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then be used to identify and isolate peptides from banks of chemically or biologically produced peptides. The isolated peptides would then act as the pharmacore.

By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available to perform such analytical studies as X-ray crystallography. In addition, knowledge of the PRO polypeptide amino acid sequence provided herein will provide guidance to those employing computer modeling techniques in place of or in addition to x-ray crystallography.

Deposit of Material

The following materials have been deposited with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209, USA (ATCC):

Table 2

		1 able 2	•
5	Material	ATCC Dep. No.	Deposit Date
	DNA16422-1209	209929	June 2, 1998
	DNA16435-1208	209930	June 2, 1998
	DNA21624-1391	209917	June 2, 1998
	DNA23334-1392	209918	June 2, 1998
10	DNA26288-1239	209792	April 21, 1998
	DNA26843-1389	203099	August 4, 1998
	DNA26844-1394	209926	June 2, 1998
	DNA30862-1396	209920	June 2, 1998
	DNA35680-1212	209790	April 21, 1998
15	DNA40621-1440	209922	June 2, 1998
	DNA44161-1434	209907	May 27, 1998
	DNA44694-1500	203114	August 11, 1998
	DNA45495-1550	203156	August 25, 1998
	DNA47361-1154	209431	November 7, 1997
20	DNA47394-1572	203109	August 11, 1998
	DNA48320-1433	209904	May 27, 1998
	DNA48334-1435	209924	June 2, 1998
	DNA48606-1479	203040	July 1, 1998
	DNA49141-1431	203003	June 23, 1998
25	DNA49142-1430	203002	June 23, 1998
	DNA49143-1429	203013	June 23, 1998
	DNA49647-1398	209919	June 2, 1998
	DNA49819-1439	209931	June 2, 1998
	DNA49820-1427	209932	June 2, 1998
-30 -	DNA49821-1562	209981	June 16, 1998
	DNA52192-1369	203042	July 1, 1998
	DNA52598-1518	203107	August 11, 1998
	DNA53913-1490	203162	August 25, 1998
	DNA53978-1443	209983	June 16, 1998
. 35	DNA53996-1442	209921	June 2, 1998
	DNA56041-1416	203012	June 23, 1998
	DNA56047-1456	209948	June 9, 1998
	DNA56050-1455	203011	June 23, 1998
	DNA56110-1437	203113	August 11, 1998
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	DNA56410-1414	209923	June 2, 1998
	DNA56436-1448	209902	May 27, 1998
	DNA56855-1447	203004	June 23, 1998
	DNA56859-1445	203019	June 23, 1998
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	DNA56865-1491	203022	June 23, 1998
	DNA56866-1342	203023	June 23, 1998
	DNA56868-1209	203024	June 23, 1998
	DNA56869-1545	203161	August 25, 1998
50	DNA56870-1492	209925	June 2, 1998
	DNA57033-1403	209905	May 27, 1998
	DNA57037-1444	209903	May 27, 1998
	DNA57129-1413	209977	June 16, 1998

		209950	June 9, 1998
	DNA57690-1374	203008	June 23, 1998
	DNA57693-1424	203017	June 23, 1998
	DNA57694-1341	203006	June 23, 1998
	DNA57695-1340	203020	June 23, 1998
_	DNA57699-1412	209951	June 9, 1998
5	DNA57702-1476	209953	June 9, 1998
	DNA57704-1452	203021	June 23, 1998
	DNA57708-1411	203021	July 1, 1998
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	DNA57711-1501	203047	July 1, 1998
10	DNA57827-1493	209954	June 9, 1998
	DNA57834-1339		June 23, 1998
	DNA57836-1338	203025	June 23, 1998
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	DNA57844-1410	203010	August 11, 1998
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	DNA58723-1588	203133	August 18, 1998
	DNA58737-1473	203136	August 25, 1998
	DNA58743-1609	203154	June 9, 1998
	DNA58846-1409	209957	June 9, 1998
20	DNA58848-1472	209955	June 9, 1998
	DNA58849-1494	209958	June 9, 1998
	DNA58850-1495	209956	June 23, 1998
	DNA58853-1423	203016	June 23, 1998
	DNA58855-1422	203018	June 23, 1998
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	DNA59211-1450	209960	June 9, 1998
	DNA59213-1487	209959	July 1, 1998
	DNA59214-1449	203046	June 9, 1998
	DNA59215-1425	209961	June 9, 1998
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	DNA59497-1496	209941	August 11, 1998
	DNA59588-1571	203106	June 9, 1998
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	DNA59605-1418	203005	June 9, 1998
	DNA59606-1471	209945	June 9, 1998
	DNA59607-1497	209957	June 9, 1998
	DNA59609-1470	209963	June 16, 1998
40	DNA59610-1559	209990	June 9, 1998
	DNA59612-1466	209947	June 23, 1998
	DNA59613-1417	203007	June 16, 1998
	DNA59616-1465	209991	July 1, 1998
	DNA59619-1464	203041	June 16, 1998
45		209989	June 17, 1998
	DNA59625-1498	209992	August 11, 1998
	DNA59767-1489	203108	August 18, 1998
	DNA59776-1600	203128	August 11, 1998
	DNA59777-1480	203111	August 18, 1998
50	DNA59820-1549	203129	August 4, 1998
	DNA59827-1426	203089	August 4, 1998 August 25, 1998
	DNA59828-1608	203158	
	DNA59838-1462	209976	June 16, 1998
	DNA59839-1461	209988	June 16, 1998
5:		203044	July 1, 1998
٠.	DNA59842-1502	209982	June 16, 1998
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	DNA59846-1503	209978	June 16, 1998
	DNA59847-1511	203098	August 4, 1998
	DNA59848-1512	203088	August 4, 1998
	DNA59849-1504	209986	June 16, 1998
	DNA59853-1505	209985	June 16, 1998
5	DNA59854-1459	209974	June 16, 1998
	DNA60283-1484	203043	July 1, 1998
	DNA60615-1483	209980	June 16, 1998
	DNA60619-1482	209993	June 16, 1998
	DNA60621-1516	203091	August 4, 1998
10	DNA60622-1525	203090	August 4, 1998
	DNA60625-1507	209975	June 16, 1998
	DNA60627-1508	203092	August 4, 1998
	DNA60629-1481	209979	June 16, 1998
	DNA61755-1554	203112	August 11, 1998
15	DNA61873-1574	203132	August 18, 1998
	DNA62814-1521	203093	August 4, 1998
	DNA62872-1509	203100	August 4, 1998
	DNA62876-1517	203095	August 4, 1998
	DNA62881-1515	203096	August 4, 1998
20	DNA64852-1589	203127	August 18, 1998
	DNA64884-1527	203155	August 25, 1998
	DNA64890-1612	203131	August 18, 1998
	DNA65412-1523	203094	August 4, 1998
	DNA66308-1537	203159	August 25, 1998
25	DNA66309-1538	203235	September 15, 1998
	DNA67004-1614	203115	August 11, 1998
	DNA68869-1610	203164	August 25, 1998
	DNA68872-1620	203160	August 25, 1998
	DNA71159-1617	203135	August 18, 1998
30			

These deposit were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement 35 between Genentech, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC §122 and the Commissioner's rules pursuant thereto (including 37 CFR §1.14 with particular reference to 886 OG 638).

The assignee of the present application has agreed that if a culture of the materials on deposit should die or be lost or destroyed when cultivated under suitable conditions, the materials will be promptly replaced on notification with another of the same. Availability of the deposited material is not to be construed as a license to practice the invention in contravention of the rights granted under the authority of any government in accordance with its patent laws.

40

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the

deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.

WHAT IS CLAIMED IS:

1. Isolated nucleic acid having at least 80% sequence identity to a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), 10 Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387). Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ

ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422) and Figure 306 (SEQ ID NO:424).

The nucleic acid sequence of Claim 1, wherein said nucleotide sequence comprises a nucleotide 2. sequence selected from the group consisting of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), 15 Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ 20 ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), 25 Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), 35 Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372),

Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421) and Figure 305 (SEQ ID NO:423).

3. The nucleic acid of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the full-length coding sequence of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEO ID NO:96), Figure 52 (SEO ID NO:98), Figure 56 (SEO ID NO:102), Figure 63 (SEO ID NO:112), Figure 65 (SEO ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEO ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEO ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID

NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421) or Figure 305 (SEQ ID NO:423).

- 4. Isolated nucleic acid which comprises the full-length coding sequence of the DNA deposited under any ATCC accession number shown in Table 2.
 - 5. A vector comprising the nucleic acid of Claim 1.
- 15 6. The vector of Claim 5 operably linked to control sequences recognized by a host cell transformed with the vector.
 - 7. A host cell comprising the vector of Claim 5.
- 20 8. The host cell of Claim 7 wherein said cell is a CHO cell.
 - 9. The host cell of Claim 7 wherein said cell is an E. coli.
 - 10. The host cell of Claim 7 wherein said cell is a yeast cell.

25

- 11. A process for producing a PRO polypeptides comprising culturing the host cell of Claim 7 under conditions suitable for expression of said PRO polypeptide and recovering said PRO polypeptide from the cell culture.
- 12. Isolated PRO polypeptide having at least 80% sequence identity to an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68

(SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ 5 ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEO ID NO:221). 10 Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422) and Figure 306 (SEQ ID NO:424).

13. Isolated PRO polypeptide having at least 80% sequence identity to the amino acid sequence encoded by a nucleic acid molecule deposited under any ATCC accession number shown in Table 2.

35

14. A chimeric molecule comprising a polypeptide according to Claim 12 fused to a heterologous amino acid sequence.

15. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is an epitope tag sequence.

- 16. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is a Fc region of an immunoglobulin.
 - An antibody which specifically binds to a PRO polypeptide according to Claim 12.
 - 18. The antibody of Claim 17 wherein said antibody is a monoclonal antibody.
- 10 19. The antibody of Claim 17 wherein said antibody is a humanized antibody.

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- 20. The antibody of Claim 17 wherein said antibody is an antibody fragment.
- An isolated nucleic acid molecule which has at least 80% sequence identity to a nucleic acid 21. which comprises a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID 15 NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), 20 Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure

191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID 5 NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 10 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID 15 NO:419), Figure 303 (SEQ ID NO:421) and Figure 305 (SEQ ID NO:423).

22. An isolated nucleic acid molecule which has at least 80% sequence identity to the full-length coding sequence of a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID 20 NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID 25 NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID 30 NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 35 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEO ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID

NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID 10 NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 15 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421) and Figure 305 (SEQ ID NO:423).

- 20 23. An isolated extracellular domain of of PRO polypeptide.
 - An isolated PRO polypeptide lacking its associated signal peptide.
- 25. An isolated polypeptide having at least about 80% amino acid sequence identity to an extracellular domain of of PRO polypeptide.
 - 26. An isolated polypeptide having at least about 80% amino acid sequence identity to a PRO polypeptide lacking its associated signal peptide.

1/310

FIGURE 1

 ${\tt CGGACGCGTGGGTGCGAGGCGAAGGTGACCGGGGACCGAGCATTTCAGATCTGCTCGGTAGA}$ ${\tt CCTGGTGCACCACCACCATG}{\tt TTGGCTGCAAGGCTGGTGTGTCTCCGGACACTACCTTCTAGG}$ GTTTTCCACCCAGCTTTCACCAAGGCCTCCCCTGTTGTGAAGAATTCCATCACGAAGAATCA ATGGCTGTTAACACCTAGCAGGGAATATGCCACCAAAACAAGAATTGGGATCCGGCGTGGGA GAACTGGCCAAGAACTCAAAGAGGCAGCATTGGAACCATCGATGGAAAAAATATTTAAAATT GATCAGATGGGAAGATGGTTTGTTGCTGGAGGGGCTGCTGTTGGTCTTGGAGCATTGTGCTA CTATGGCTTGGGACTGTCTAATGAGATTGGAGCTATTGAAAAGGCTGTAATTTGGCCTCAGT ATGTCAAGGATAGAATTCATTCCACCTATATGTACTTAGCAGGGAGTATTGGTTTAACAGCT TTGTCTGCCATAGCAATCAGCAGAACGCCTGTTCTCATGAACTTCATGATGAGAGGCTCTTG GGTGACAATTGGTGTGACCTTTGCAGCCATGGTTGGAGCTGGAATGCTGGTACGATCAATAC CATATGACCAGAGCCCAGAGCATCTTGCTTGGTTGCTACATTCTGGTGTGATGGGT GCAGTGGTGGCTCTCTGACAATATTAGGGGGTCCTCTTCTCATCAGAGCTGCATGGTACAC AGCTGGCATTGTGGGAGGCCTCTCCACTGTGGCCCATGTGTGCGCCCCAGTGAAAAGTTTCTGA ACATGGGTGCACCCCTGGGAGTGGGCCTGGGTCTCGTCTTTGTGTCCTCATTGGGATCTATG TTTCTTCCACCTACCACCGTGGCTGGTGCCACTCTTTACTCAGTGGCAATGTACGGTGGATT AGTTCTTTTCAGCATGTTCCTTCTGTATGATACCCAGAAAGTAATCAAGCGTGCAGAAGTAT CACCAATGTATGGAGTTCAAAAATATGATCCCATTAACTCGATGCTGAGTATCTACATGGAT <u>AAGTGACTCAGCTTCTGGCTTCTGCTACATCAAATATCTTGTTTAATGGGGCAGATATGC</u> ATTAAATAGTTTGTACAAGCAGCTTTCGTTGAAGTTTAGAAGATAAGAAACATGTCATCATA TTTAAATGTTCCGGTAATGTGATGCCTCAGGTCTGCCTTTTTTTCTGGAGAATAAATGCAGT AATCCTCTCCCAAATAAGCACACACATTTTCAATTCTCATGTTTGAGTGATTTTAAAATGTT TTGGTGAATGTGAAAACTAAAGTTTGTGTCATGAGAATGTAAGTCTTTTTTCTACTTTAAAA TTTAGTAGGTTCACTGAGTAACTAAAATTTAGCAAACCTGTGTTTGCATATTTTTTTGGAGT GCAGAATATTGTAATTAATGTCATAAGTGATTTGGAGCTTTGGTAAAGGGACCAGAGAGAAG GAGTCACCTGCAGTCTTTTGTTTTTTTAAATACTTAGAACTTAGCACTTGTGTTATTGATTA GCTGAACTTAACAAAACTGTTCATCCTGAAACAGGCACAGGTGATGCATTCTCCTGCTGTTG CTTCTCAGTGCTCTCTTTCCAATATAGATGTGGTCATGTTTGACTTGTACAGAATGTTAATC ATACAGAGAATCCTTGATGGAATTATATATGTGTGTTTTACTTTTGAATGTTACAAAAGGAA ATAACTTTAAAACTATTCTCAAGAGAAAATATTCAAAGCATGAAATATGTTGCTTTTTCCAG **AATACAAACAGTATACTCATG**

MLAARLVCLRTLPSRVFHPAFTKASPVVKNSITKNQWLLTPSREYATKTRIGIRRGRTGQEL KEAALEPSMEKIFKIDQMGRWFVAGGAAVGLGALCYYGLGLSNEIGAIEKAVIWPQYVKDRI HSTYMYLAGSIGLTALSAIAISRTPVLMNFMMRGSWVTIGVTFAAMVGAGMLVRSIPYDQSP GPKHLAWLLHSGVMGAVVAPLTILGGPLLIRAAWYTAGIVGGLSTVAMCAPSEKFLNMGAPL GVGLGLVFVSSLGSMFLPPTTVAGATLYSVAMYGGLVLFSMFLLYDTQKVIKRAEVSPMYGV QKYDPINSMLSIYMDTLNIFMRVATMLATGGNRKK

GAAGGCTGCCTCGCTGGTCCGAATTCGGTGGCGCCACGTCCGCCCTCTCCGCCTTCTGCAT ${\tt GGTCGGCACGGGGGGTCTTGTGCATCTTGGCTACCTGTGGGTCGAAG} {\tt ATGTCGG}$ $ACATCGGAGACTGGTTCAGGAGCATCCCGGCGATCACGCGCTATTGGTTCGCCGC\overline{CAC}CGTC$ GCCGTGCCCTTGGTCGGCAAACTCGGCCTCATCAGCCCGGCCTACCTCTTCCTCTGGCCCGA AGCCTTCCTTTATCGCTTTCAGATTTGGAGGCCAATCACTGCCACCTTTTATTTCCCTGTGG GTCCAGGAACTGGATTTCTTTATTTGGTCAATTTATATTTCTTATATCAGTATTCTACGCGA GATTTGCATCGTGATTACTGGCTTAGCAATGGATATGCAGTTGCTGATGATTCCTCTGATCA TGTCAGTACTTTATGTCTGGGCCCAGCTGAACAGAGACATGATTGTATCATTTTGGTTTGGA ACACGATTTAAGGCCTGCTATTTACCCTGGGTTATCCTTGGATTCAACTATATCATCGGAGG CTCGGTAATCAATGAGCTTATTGGAAATCTGGTTGGACATCTTTATTTTTTCCTAATGTTCA GATACCCAATGGACTTGGGAGGAAGAAATTTTCTATCCACACCTCAGTTTTTGTACCGCTGG CTGCCCAGTAGGAGGAGGAGTATCAGGATTTGGTGTGCCCCCTGCTAGCATGAGGCGAGC TGCTGATCAGAATGGCGGAGGCGGGAGACACAACTGGGGCCCAGGGCTTTCGACTTGGAGACC AGTGAAGGGGCGGCCTCGGGCAGCCGCTCCTCAAGCCACATTTCCTCCCAGTGCTGGGTG CACTTAACAACTGCGTTCTGGCTAACACTGTTGGACCTGACCCACACTGAATGTAGTCTTTC AGTACGAGACAAAGTTTCTTAAATCCCGAAGAAAAATATAAGTGTTCCACAAGTTTCACGAT TCTCATTCAAGTCCTTACTGCTGTGAAGAACAAATACCAACTGTGCAAATTGCAAAACTGAC TACATTTTTTGGTGTCTTCTCTCTCTCCCCTTTCCGTCTGAATAATGGGTTTTTAGCGGGTCCT AATCTGCTGGCATTGAGCTGGGGCTGGGTCACCAAACCCTTCCCAAAAGGACCTTATCTCTT TCTTGCACACATGCCTCTCTCCCACTTTTCCCAACCCCCACATTTGCAACTAGAAAAAGTTG ACAACAATCATATTCACGTTATTTTCCCCTTTTGGTGGCAGAACTGTTACCAATAGGGGGAG ${\tt AAGACAGCCACGGATGAAGCGTTTCTCAGCTTTTGGAATTGCTTCGACTGACATCCGTTGTT}$ AACCGTTTGCCACTCTTCAGATATTTTTTATAAAAAAAGTACCACTGAGTTCATGAGGGCCA TCAAGACTGTAGTGGAGTTGCAGCTAACATGGGTTAGGTTTAAACCATGGGGGATGCACCCC TTTGCGTTTCATATGTAGCCCTACTGGCTTTGTGTAGCTGGAGTAGTTGGGTTGCTTTGTGT TAGGAGGATCCAGATCATGTTGGCTACAGGGAGATGCTCTCTTTGAGAGGTCCTGGGCATTG ATTCCCATTTCAATCTCATTCTGGATATGTGTTCATTGAGTAAAGGAGGAGAGACCCTCATA GAGGAAGGCGCAGCTCCTCTCTGCACGTAGATCATTTTTTAAAGCTAATGTAAGCACATCTA AGGGAATAACATGATTTAAGGTTGAAATGGCTTTAGAATCATTTGGGTTTGAGGGTGTGTTA TTTTGAGTCATGAATGTACAAGCTCTGTGAATCAGACCAGCTTAAATACCCACACCTTTTTT TCGTAGGTGGGCTTTTCCTATCAGAGCTTGGCTCATAACCAAATAAAGTTTTTTGAAGGCCA TGGCTTTTCACACAGTTATTTTATTTTATGACGTTATCTGAAAGCAGACTGTTAGGAGCAGT ATTGAGTGGCTGTCACACTTTGAGGCAACTAAAAAGGCTTCAAACGTTTTGATCAGTTTCTT TTCAGGAAACATTGTGCTCTAACAGTATGACTATTCTTTCCCCCCACTCTTAAACAGTGTGAT GTGTGTTATCCTAGGAAATGAGAGTTGGCAAACAACTTCTCATTTTGAATAGAGTTTGTGTG TACTTCTCCATATTTAATTTATATGATAAAATAGGTGGGGAGAGTCTGAACCTTAACTGTCA TGTTTTGTTGTTCATCTGTGGCCACAATAAAGTTTACTTGTAAAATTTTAGAGGCCATTACT CAGTCATTTTTCCTAAAGGTTTACAAGTATTTAGAACTTTTCAGTTCAGGGCAAAATGTTC ATGAAGTTATTCCTCTTAAACATGGTTAGGAAGCTGATGACGTTATTGATTTTGTCTGGATT ATGTTTCTGGAATAATTTTACCAAAACAAGCTATTTGAGTTTTGACTTGACAAGGCAAAACA TGACAGTGGATTCTCTTTACAAATGGAAAAAAAAAATCCTTATTTTGTATAAAGGACTTCCC TTTTTGTAAACTAATCCTTTTTATTGGTAAAAATTGTAAATTAAAATGTGCAACTTG

MSDIGDWFRSIPAITRYWFAATVAVPLVGKLGLISPAYLFLWPEAFLYRFQIWRPITATFYF PVGPGTGFLYLVNLYFLYQYSTRLETGAFDGRPADYLFMLLFNWICIVITGLAMDMQLLMIP LIMSVLYVWAQLNRDMIVSFWFGTRFKACYLPWVILGFNYIIGGSVINELIGNLVGHLYFFL MFRYPMDLGGRNFLSTPQFLYRWLPSRRGGVSGFGVPPASMRRAADQNGGGGRHNWGQGFRLGDQ

GGGGCCGCGGTCTAGGGCGGCTACGTGTTGTTGCCATAGCGACCATTTTGCATTAACTGGTTG GTAGCTTCTATCCTGGGGGCTGAGCGACTGCGGGCCAGCTCTTCCCCTACTCCCTCTCGGCT CCTTGTGGCCCAAAGGCCTAACCGGGGTCCGGCGTCTGGCCTAGGGATCTTCCCCGTTGCC CCTTTGGGGCGGATGCCTGCGGAAGAAGAAGACGAGGTGGATGGGTAGTGGAGAGCATCG CGGGGTTCCTGCGAGGCCCAGACTGGTCCATCCCCATCTTGGACTTTGTGGAACAGAAATGT GAAGTTAACTGCAAAGGAGGCATGTGATAACTCCAGGAAGCCCAGAGCCGGTGATTTTGGT GGCCTGTGTTCCCCTTGTTTTTGATGATGAAGAAGAAAGCAAATTGACCTATACAGAGATTC ATCAGGAATACAAAGAACTAGTTGAAAAGCTGTTAGAAGGTTACCTCAAAGAAATTGGAATT AATGAAGATCAATTTCAAGAAGCATGCACTTCTCCTCTTGCAAAGACCCATACATCACAGGC CATTTTGCAACCTGTGTTGGCAGCAGAAGATTTTACTATCTTTAAAGCAATGATGGTCCAGA AAAACATTGAAATGCAGCTGCAAGCCATTCGAATAATTCAAGAGAGAAATGGTGTATTACCT GACTGCTTAACCGATGGCTCTGATGTGGTCAGTGACCTTGAACACGAAGAGATGAAAATCCT GAGGGAAGTTCTTAGAAAATCAAAAGAGGAATATGACCAGGAAGAAGAAAGGAAGAGAGAAAA **AACAGTTATCAGAGGCTAAAACAGAAGAGCCCACAGTGCATTCCAGTGAAGCTGCAATAATG** CACAAAAAGGCCTGAAGATTCCTGGCTTAGAGCATGCGAGCATTGAAGGACCAATAGCAAAC TTATCAGTACTTGGAACAGAAGAACTTCGGCAACGAGAACACTATCTCAAGCAGAAGAGAGA TAAGTTGATGTCCATGAGAAAGGATATGAGGACTAAACAGATACAAAATATGGAGCAGAAAG GAAAACCCACTGGGGAGGTAGAGGAAATGACAGAGAAACCAGAAATGACAGCAGAGGAGAAG CAAACATTACTAAAGAGGAGATTGCTTGCAGAGAAACTCAAAGAAGAAGTTATTAATAAGTA CTTACACTG

6/310

FIGURE 6

MAAEEEDEVEWVVESIAGFLRGPDWSIPILDFVEQKCEVNCKGGHVITPGSPEPVILVACVP LVFDDEEESKLTYTEIHQEYKELVEKLLEGYLKEIGINEDQFQEACTSPLAKTHTSQAILQP VLAAEDFTIFKAMMVQKNIEMQLQAIRIIQERNGVLPDCLTDGSDVVSDLEHEEMKILREVL RKSKEEYDQEEERKRKKQLSEAKTEEPTVHSSEAAIMNNSQGDGEHFAHPPSEVKMHFANQS IEPLGRKVERSETSSLPQKGLKIPGLEHASIEGPIANLSVLGTEELRQREHYLKQKRDKLMS MRKDMRTKQIQNMEQKGKPTGEVEEMTEKPEMTAEEKQTLLKRRLLAEKLKEEVINK

GGGCACAGCACATGTGAAGTTTTTGATGATGAAGAAGAAAGCAAATTGACCTATACAGAGAT
TCATCAGGAATACAAAGAACTAGTTGAAAAAGCTGTTAGAAGGTTACCTCAAAGAAATTGGAA
TTAATGAAGATCAATTTCAAGAAGCATGCACTTCTCCTCTTGCAAAGACCCATACATCACAG
GCCATTTTTGCAACCTGTGTTGGCAGCAGAAGATTTTACTATCTTTAAAGCAATGATGGTCC
AGAAAAACATTGAAATGCAGCTGCAAGCCATTCGAATAATTCAAGAGAGAAAATGGTGTATTA
CCTGACTGCTTAACCGATGGCTCTGATGTGGTCAGTGACCTTGAACACGAAGAGATGAAAAT
CCTGAGGGAAGTTCTTAGAAAATCAAAAGAGGAATATGACCAGGAA

TAGCTTCTCCACGTATGGACCCTAAAGGCTACTGCTGCTACTACGGGGCTAGACAGTTACTG AGTGGA<u>ATG</u>GAAAAACAGTGCTGTAGTCATCCTGTAATATGCTCCTTGTCAACAATGTATAC ATTCCTGCTAGGTGCCATATTCATTGCTTTAAGCTCAAGTCGCATCTTACTAGTGAAGTATT CTGCCAATGAAGAAAACAAGTATGATTATCTTCCAACTACTGTGAATGTGTGCTCAGAACTG AAATTTGAAATATGCTTCCTGGAAGGAATTCTCTGATTTCATGAAGTGGTCCATTCCTGCCT TTCTTTATTTCCTGGATAACTTGATTGTCTTCTATGTCCTGTCCTATCTTCAACCAGCCATG GCTGTTATCTTCTCAAATTTTAGCATTATAACAACAGCTCTTCTATTCAGGATAGTGCTGAA GAGGCGTCTAAACTGGATCCAGTGGGCTTCCCTCCTGACTTTATTTTTTGTCTATTGTGGCCT TGACTGCCGGGACTAAAACTTTACAGCACAACTTGGCAGGACGTGGATTTCATCACGATGCC TACAGCAAAGGAATGGACTTTTCCTGAAGCTAAATGGAACACCACAGCCAGAGTTTTCAGTC ACATCCGTCTTGGCATGGCCATGTTCTTATTATAGTCCAGTGTTTTATTTCTTCAATGGCT AATATCTATAATGAAAAGATACTGAAGGAGGGGAACCAGCTCACTGAAAGCATCTTCATACA GAACAGCAAACTCTATTTCTTTGGCATTCTGTTTAATGGGCTGACTCTGGGCCTTCAGAGGA CTTATTTTTGTAACTGCATTCCAGGGCCTTTCAGTGGCTTTCATTCTGAAGTTCCTGGATAA TCTTTGACTTCAGGCCCTCCCTGGAATTTTTCTTGGAAGCCCCATCAGTCCTTCTCTATA TTTATTTATAATGCCAGCAAGCCTCAAGTTCCGGAATACGCACCTAGGCAAGAAAGGATCCG AGATCTAAGTGGCAATCTTTGGGAGCGTTCCAGTGGGGATGGAGAAGAACTAGAAAGACTTA $\tt CCAAACCCAAGAGTGATGAGTCAGATGAAGATACTTTC\underline{TAA}CTGGTACCCACATAGTTTGCA$ GCTCTCTTGAACCTTATTTTCACATTTTCAGTGTTTGTAATATTTATCTTTTCACTTTGATA AACCAGAAATGTTTCTAAATCCTAATATTCTTTGCATATATCTAGCTACTCCCTAAATGGTT CCATCCAAGGCTTAGAGTACCCAAAGGCTAAGAAATTCTAAAGAACTGATACAGGAGTAACA ATATGAAGAATTCATTAATATCTCAGTACTTGATAAATCAGAAAGTTATATGTGCAGATTAT TTTCCTTGGCCTTCAAGCTTCCAAAAAACTTGTAATAATCATGTTAGCTATAGCTTGTATAT ACACATAGAGATCAATTTGCCAAATATTCACAATCATGTAGTTCTAGTTTACATGCCAAAGT CTTCCCTTTTTAACATTATAAAAGCTAGGTTGTCTCTTGAATTTTGAGGCCCTAGAGATAGT CTGGCCATACCATAGATTTGGGATGATGTAGTCTGTGCTAAATATTTTGCTGAAGAAGCAGT TTCTCAGACACAACATCTCAGAATTTTAATTTTTAGAAATTCATGGGAAATTGGATTTTTGT AATAATCTTTTGATGTTTTAAACATTGGTTCCCTAGTCACCATAGTTACCACTTGTATTTTA AGTCATTTAAACAAGCCACGGTGGGGCTTTTTTCTCCTCAGTTTGAGGAGAAAAATCTTGAT AATTCAAGCTGTGACTATTGTATATCTTTCCAAGAGTTGAAATGCTGGCTTCAGAATCATAC CAGATTGTCAGTGAAGCTGATGCCTAGGAACTTTTAAAGGGATCCTTTCAAAAGGATCACTT AGCAAACACATGTTGACTTTTAACTGATGTATGAATATTAATACTCTAAAAATAGAAAGACC AGTAATATAAAGTCACTTTACAGTGCTACTTCACACTTAAAAGTGCATGGTATTTTTCATG GTATTTTGCATGCAGCCAGTTAACTCTCGTAGATAGAGAAGTCAGGTGATAGATGATATTAA AAATTAGCAAACAAAAGTGACTTGCTCAGGGTCATGCAGCTGGGTGATGATAGAAGAGTGGG CTTTAACTGGCAGGCCTGTATGTTTACAGACTACCATACTGTAAATATGAGCTTTATGGTGT CATTCTCAGAAACTTATACATTTCTGCTCTCCTTTCTCCTAAGTTTCATGCAGATGAATATA AGGTAATATACTATTATATAATTCATTTGTGATATCCACAATAATATGACTGGCAAGAATTG GTGGAAATTTGTAATTAAAATAATTATTAAAACCT

MEKQCCSHPVICSLSTMYTFLLGAIFIALSSSRILLVKYSANEENKYDYLPTTVNVCSELVK LVFCVLVSFCVIKKDHQSRNLKYASWKEFSDFMKWSIPAFLYFLDNLIVFYVLSYLQPAMAV IFSNFSIITTALLFRIVLKRRLNWIQWASLLTLFLSIVALTAGTKTLQHNLAGRGFHHDAFF SPSNSCLLFRSECPRKDNCTAKEWTFPEAKWNTTARVFSHIRLGMGHVLIIVQCFISSMANI YNEKILKEGNQLTESIFIQNSKLYFFGILFNGLTLGLQRSNRDQIKNCGFFYGHSAFSVALI FVTAFQGLSVAFILKFLDNMFHVLMAQVTTVIITTVSVLVFDFRPSLEFFLEAPSVLLSIFI YNASKPQVPEYAPRQERIRDLSGNLWERSSGDGEELERLTKPKSDESDEDTF

GTGGCTAAGGCTGCTACGAAGCGAGCTTGGGAGGAGCAGCGGCCTGCGGGGCAGAGGAGCAT CCCGTCTACCAGGTCCCAAGCGGCGTGGCCCGCGGGTCATGGCCAAAGGAGAAGCCGCCGAG AGCGGCTCCGCGGGGGCTGCTACCCACCAGCATCCTCCAAAGCACTGAACGCCCGGCCCA GGTGAAGAAGAACCGAAAAAGAAGAACAACAGTTGTCTGTTTGCAACAAGCTTTGCTATG CTATTGGATGTGGCTCAGGTGGGCCCTTTCTCTGCCTCCATCATCCTGTTTGTGGGCCGAGC CTGGGATGCCATCACAGACCCCCTGGTGGGCCTCTGCATCAGCAAATCCCCCTGGACCTGCC TGGGTCGCCTTATGCCCTGGATCATCTTCTCCACGCCCCTGGCCGTCATTGCCTACTTCCTC ATCTGGTTCGTGCCCGACTTCCCACACGGCCAGACCTATTGGTACCTGCTTTTCTATTGCCT CTTTGAAACAATGGTCACGTGTTTCCATGTTCCCTACTCGGCTCTCACCATGTTCATCAGCA ACCGAGCAGACTGAGCGGGATTCTGCCACCGCCTATCGGATGACTGTGGAAGTGCTGGGCAC AGTGCTGGGCACGGCGATCCAGGGACAAATCGTGGGCCAAGCAGACACGCCTTGTTTCCAGG ACTTCAATAGCTCTACAGTAGCTTCACAAAGTGCCAACCATACACATGGCACCACTTCACAC AGGGAAACGCAAAAGGCATACCTGCTGGCAGCGGGGTCATTGTCTGTATCTATAAATCTG TGCTGTCATCCTGATCCTGGGCGTGCGGGAGCAGAGAACCCTATGAAGCCCAGCAGTCTG AGCCAATCGCCTACTTCCGGGGCCTACGGCTGGTCATGAGCCACGGCCCATACATCAAACTT ATTACTGGCTTCCTCTTCACCTCCTTGGCTTTCATGCTGGTGGAGGGGAACTTTGTCTTGTT TTGCACCTACACCTTGGGCTTCCGCAATGAATTCCAGAATCTACTCCTGGCCATCATGCTCT CGGCCACTTTAACCATTCCCATCTGGCAGTGGTTCTTGACCCGGTTTGGCAAGAAGACAGCT GTATATGTTGGGATCTCATCAGCAGTGCCATTTCTCATCTTGGTGGCCCTCATGGAGAGTAA CCTCATCATTACATATGCGGTAGCTGTGGCAGCTGGCATCAGTGTGGCAGCTGCCTTCTTAC TACCCTGGTCCATGCTGCCTGATGTCATTGACGACTTCCATCTGAAGCAGCCCCACTTCCAT GGAACCGAGCCCATCTTCTTCTCCTTCTATGTCTTCTTCACCAAGTTTGCCTCTGGAGTGTC ACTGGGCATTTCTACCCTCAGTCTGGACTTTGCAGGGTACCAGACCCGTGGCTGCTCGCAGC CGGAACGTGTCAAGTTTACACTGAACATGCTCGTGACCATGGCTCCCATAGTTCTCATCCTG GGCCCTGCAGGCACTGAGGGACGAGGCCAGCAGCTCTGGCTGAGAAACAGACTCCACAG AGCTGGCTAGCATCCTCTAGGGCCCGCCACGTTGCCCGAAGCCACCATGCAGAAGGCCACAC AAGGGATCAGGACCTGTCTGCCGGCTTGCTGAGCAGCTGGACTGCAGGTGCTAGGAAGGGAA CTGAAGACTCAAGGAGGTGGCCCAGGACACTTGCTGTGCTCACTGTGGGGCCGGCTGCTCTG TGGCCTCCTGCCTCTGCCTGCCTGTGGGGCCAAGCCCTGGGGCTGCCACTGTGAATA TTAATGTTATTAATTTTCATAAAAGCTGGAAAGC

MWLRWALSLPPSSCLWAEPGMPSQTPWWASASANPPGPAWVALCPGSSSPRPWPSLPTSSSG
SCPTSHTARPIGTCFSIASLKQWSRVSMFPTRLSPCSSATEQTERDSATAYRMTVEVLGTVL
GTAIQGQIVGQADTPCFQDFNSSTVASQSANHTHGTTSHRETQKAYLLAAGVIVCIYIICAV
ILILGVREQREPYEAQQSEPIAYFRGLRLVMSHGPYIKLITGFLFTSLAFMLVEGNFVLFCT
YTLGFRNEFQNLLLAIMLSATLTIPIWQWFLTRFGKKTAVYVGISSAVPFLILVALMESNLI
ITYAVAVAAGISVAAAFLLPWSMLPDVIDDFHLKQPHFHGTEPIFFSFYVFFTKFASGVSLG
ISTLSLDFAGYQTRGCSQPERVKFTLNMLVTMAPIVLILLGLLLFKMYPIDEERRRQNKKAL
QALRDEASSSGCSETDSTELASIL

GGGAAACGCAAAAGGCATACCTGCTGGCAGCGGGGGTCATTGTCTGTATCTATATAATCTGT
GCTGTCATCCTGATCCTGGGCGTGCGGGAGCAGAGAACCCTATGAAGCCCAGCAGTCTGA
GCCAATCGCCTACTTCCGGGGCCTACGGCTGGTCATGAGCCACGGCCCATACATCAAACTTA
TTACTGGCTTCCTCTTCACCTCCTTGGCTTTCATGCTGGTGGAGGGGAACTTTGTCTTGTTT
TGCACCTACACCTTGGGCTTCCGCAATGAATTCCAGAATCTACTCCTGGCCATCATGCTCTC
GGCCACTTTAACCATTCCCATCTGGCAGTGGTTCTTGACCCGGTTTGGCAAGAAGACAGCTG
TATATGTTGGGATCTCATCAGCAGTGCCATTTCTCATCTTGGTGGCCCCTCATGGAGAGTAAC
CTCATCATTACATATGCGGTAGCTGTGGCAGCTGGCATCAGTGTGGCAGCTGCCTTCTTACT
ACCCTGGTCCATGCTGCCTGATGTCATTGACGACTTCCATCTGAAGCAGCCCCCACTTCCATG

GGGGCTTCGGCGCCAGCGCCAGCGCTAGTCGGTCTGGTAAGGATTTACAAAAGGTGCAGGT ATGAGCAGGTCTGAAGACTAACATTTTGTGAAGTTGTAAAACAGAAAACCTGTTAGAA<u>ATG</u>T GGTGGTTTCAGCAAGGCCTCAGTTTCCTTCCTTCAGCCCTTGTAATTTGGACATCTGCTGCT TTCATATTTTCATACATTACTGCAGTAACACTCCACCATATAGACCCGGCTTTACCTTATAT CAGTGACACTGGTACAGTAGCTCCAGAAAAATGCTTATTTGGGGCAATGCTAAATATTGCGG CAGTTTTATGCATTGCTACCATTTATGTTCGTTATAAGCAAGTTCATGCTCTGAGTCCTGAA GAGAACGTTATCATCAAATTAAACAAGGCTGGCCTTGTACTTGGAATACTGAGTTGTTTAGG ACTTTCTATTGTGGCAAACTTCCAGAAAACAACCCTTTTTGCTGCACATGTAAGTGGAGCTG TGCTTACCTTTGGTATGGGCTCATTATATATGTTTGTTCAGACCATCCTTTCCTACCAAATG CAGCCCAAAATCCATGGCAAACAAGTCTTCTGGATCAGACTGTTGTTGGTTATCTGGTGTGG AGTAAGTGCACTTAGCATGACTTGCTCATCAGTTTTGCACAGTGGCAATTTTGGGACTG ATTTAGAACAGAAACTCCATTGGAACCCCGAGGACAAAGGTTATGTGCTTCACATGATCACT ACTGCAGCAGAATGGTCTATGTCATTTTCCTTCTTTTGGTTTTTTCCTGACTTACATTCGTGA TTTTCAGAAAATTTCTTTACGGGTGGAAGCCAATTTACATGGATTAACCCTCTATGACACTG CACCTTGCCCTATTAACAATGAACGAACACGGCTACTTTCCAGAGATATT<u>TGA</u>TGAAAGGAT AAAATATTTCTGTAATGATTATGATTCTCAGGGATTGGGGAAAGGTTCACAGAAGTTGCTTA TTCTTCTCTGAAATTTTCAACCACTTAATCAAGGCTGACAGTAACACTGATGAATGCTGATA ATCAGGAAACATGAAAGAAGCCATTTGATAGATTATTCTAAAGGATATCATCAAGAAGACTA TTAAAAACACCTATGCCTATACTTTTTTATCTCAGAAAATAAAGTCAAAAGACTATG

MWWFQQGLSFLPSALVIWTSAAFIFSYITAVTLHHIDPALPYISDTGTVAPEKCLFGAMLNI
AAVLCIATIYVRYKQVHALSPEENVIIKLNKAGLVLGILSCLGLSIVANFQKTTLFAAHVSG
AVLTFGMGSLYMFVQTILSYQMQPKIHGKQVFWIRLLLVIWCGVSALSMLTCSSVLHSGNFG
TDLEQKLHWNPEDKGYVLHMITTAAEWSMSFSFFGFFLTYIRDFQKISLRVEANLHGLTLYD
TAPCPINNERTRLLSRDI

16/3-10

FIGURE 16

CCCACGCGTCCGCCGCCGCGCGCGCGCGCGCGGGGGCTGCCCCGCGGG $\tt CCGGGGTGCGGAGCCGAC{\underline{ATG}}CGCCCGCTTCTCGGCCTCCTTCTGGTCTTCGCCGGCTGCAC$ CTTCGCCTTGTACTTGCTGTCGACGCGACTGCCCCGCGGGGGGAGACTGGGCTCCACCGAGG AGGCTGGAGGCAGGTCGCTGTGGTTCCCCTCCGACCTGGCAGAGCTGCGGGAGCTCTCTGAG GTCCTTCGAGAGTACCGGAAGGAGCACCAGGCCTACGTGTTCCTGCTCTTCTGCGGCGCCCTA CCTCTACAAACAGGGCTTTGCCATCCCGGCTCCAGCTTCCTGAATGTTTTAGCTGGTGCCT TGCTACCTGCTCTCCAGTATTTTTGGCAAACAGTTGGTGGTGTCCTACTTTCCTGATAAAGT TGAGACTTTTCCCCATGACACCAAACTGGTTCTTGAACCTCTCGGCCCCAATTCTGAACATT CCCATCGTGCAGTTCTTCTCAGTTCTTATCGGTTTGATCCCATATAATTTCATCTGTGT GCAGACAGGGTCCATCCTGTCAACCCTAACCTCTCTGGATGCTCTTTTCTCCTGGGACACTG TCTTTAAGCTGTTGGCCATTGCCATGGTGGCATTAATTCCTGGAACCCTCATTAAAAAATTT AGTCAGAAACATCTGCAATTGAATGAAACAAGTACTGCTAATCATATACACAGTAGAAAAGA $\texttt{CACA} \underline{\textbf{TGA}} \underline{\textbf{TCTGGATTTCTGTTTGCCACATCCCTGGACTCAGTTGCTTATTTGTGTAATGGA}$ TGTGGTCCTCTAAAGCCCCTCATTGTTTTTGATTGCCTTCTATAGGTGATGTGGACACTGTG CATCAATGTGCAGTGTCTTTTCAGAAAGGACACTCTGCTCTTGAAGGTGTATTACATCAGGT TTTCAAACCAGCCCTGGTGTAGCAGACACTGCAACAGATGCCTCCTAGAAAATGCTGTTTGT GGCCGGGCGCGGTGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCCGGTGATTC ACAAGGTCAGGAGTTCAAGACCAGCCTGGCCAAGATGGTGAAATCCTGTCTCTAATAAAAAT ACAAAAATTAGCCAGGCGTGGTGGCAGGCACCTGTAATCCCAGCTACTCGGGAGGCTGAGGC AGGAGAATTGCTTGAACCAAGGTGGCAGAGGTTGCAGTAAGCCAAGATCACACCACTGCACT CCAGCCTGGGTGATAGAGTGAGACACTGTCTTGAC

MRPLLGLLLVFAGCTFALYLLSTRLPRGRRLGSTEEAGGRSLWFPSDLAELRELSEVLREYR
KEHQAYVFLLFCGAYLYKQGFAIPGSSFLNVLAGALFGPWLGLLLCCVLTSVGATCCYLLSS
IFGKQLVVSYFPDKVALLQRKVEENRNSLFFFLLFLRLFPMTPNWFLNLSAPILNIPIVQFF
FSVLIGLIPYNFICVQTGSILSTLTSLDALFSWDTVFKLLAIAMVALIPGTLIKKFSQKHLQ
LNETSTANHIHSRKDT

19/310

FIGURE 19

CCGAGGCGGGAGGAGCCCGAGGGGGGGCGCGAGCCCCGCATGAATCATTGTAGTCAATCATTTT CCAGTTCTCAGCCGCTCAGTTGTGATCAAGGGACACGTGGTTTCCGAACTGCCAGCTCAGAA TAGGAAAATAACTTGGGATTTTATATTGGAAGACATGGATCTTGCTGCCAACGAGATCAGCA TCAGAGAAGGCAATTGAAAAATTTATCAGACAGCTGCTGGAAAAGAATGAACCTCAGAGACC CCCCCGCAGTATCCTCTCTTATAGTTGTGTATAAGGTTCTCGCAACCTTGGGATTAATCT TGCTCACTGCCTACTTTGTGATTCAACCTTTCAGCCCCATTAGCACCTGAGCCAGTGCTTTCT GGAGCTCACCCTGGCGCTCACTCATCCATCACATTAGGCTGATGTCCTTGCCCATTGCCAA CAGACTTTGACCCCTGGTGGACAAACGACTGTGAGCAGAATGAGTCAGAGCCCATTCCTGCC AACTGCACTGGCTGTGCCCAGAAACACCTGAAGGTGATGCTCCTGGAAGACGCCCCAAGGAA ATTTGAGAGGCTCCATCCACTGGTGATCAAGACGGGAAAGCCCCTGTTGGAGGAAGAGATTC AGCATTTTTTGTGCCAGTACCCTGAGGCGACAGAAGGCTTCTCTGAAGGGTTTTTCGCCAAG TGGTGGCGCTGCTTTCCTGAGCGGTGGTTCCCATTTCCTTATCCATGGAGGAGACCTCTGAA CCTCTTTAAACAAGTGCTCCTTTCTTCACCCAGAACCTGTTGTGGGGAGTAAGATGCATAAG GTGCCGAAGACATTGTCAGTCTGTGGCCATGCCAATAGAGCCAGGGGATATCGGCTATGTCG ACACCACCCACTGGAAGGTCTACGTTATAGCCAGAGGGGTCCAGCCTTTGGTCATCTGCGAT GGAACCGCTTTCTCAGAACTGTAGGAAATAGAACTGTGCACAGGAACAGCTTCCAGAGCCGA AAACCAGGTTGAAAGGGGAAAAATAAAAACAAAAACGATGAAACTGCAAAAA

MDLAANEISIYDKLSETVDLVRQTGHQCGMSEKAIEKFIRQLLEKNEPQRPPPQYPLLIVVY
KVLATLGLILLTAYFVIQPFSPLAPEPVLSGAHTWRSLIHHIRLMSLPIAKKYMSENKGVPL
HGGDEDRPFPDFDPWWTNDCEQNESEPIPANCTGCAQKHLKVMLLEDAPRKFERLHPLVIKT
GKPLLEEEIQHFLCQYPEATEGFSEGFFAKWWRCFPERWFPFPYPWRRPLNRSQMLRELFPV
FTHLPFPKDASLNKCSFLHPEPVVGSKMHKMPDLFIIGSGEAMLQLIPPFQCRRHCQSVAMP
IEPGDIGYVDTTHWKVYVIARGVQPLVICDGTAFSEL

FIGURE 21

FIGURE 22

CCCACGCGTCCGCCCACGCGTCCGGCTGAACACCTCTTCTTTGGAGTCAGCCACTGATGAGG CAGGGTCCCCACTTGCAGCTGCAGCAGCTGCAGCAGCTGCAGAGCGCTGCTCGTGGTG CCACTGGTGCGCACGCTGCTAGACCGTGCCTATGAGCCGCTGGGGGCTGCAGTGGGGACTGCC CTCCCTGCCACCCACTATGGCAGCCCCACCTTCTTTGAAGACTTCCAGGCTTTTTGTGCCA CACCCGAATGGCGCCACTTCATCGACAAACAGGTACAGCCAACCATGTCCCAGTTCGAAATG GACACGTATGCTAAGAGCCACGACCTTATGTCAGGTTTCTGGAATGCCTGCTATGACATGCT TATGAGCAGTGGGCAGCGCCCAGTGGGAGCGCCCCAGAGTCGTCGGGCCTTCCAGGAGC TGGTGCTGGAACCTGCGCAGAGGCGGCGCGCCTGGAGGGGCTACGCTACACGGCAGTGCTG AAGCAGCAGCAACGCAGCACTCCATGGCCCTGCTGCACTGGGGGGCGCTGTGGCGCCAGCT CGCCAGCCCATGTGGGGCCTGGGCGCTGAGGGACACTCCCATCCCCGCTGGAAACTGTCCA GCGCCGAGACATATTCACGCATGCGTCTGAAGCTGGTGCCCAACCATCACTTCGACCCTCAC CTCACTGCCTCTGGCAGTGACCAAAGAGGCCAAAGTGAGCACCCCACCCGAGTTGCTGCAGG AGGACCAGCTCGGCGAGGACGAGCTGGCTGAGCTGGAGACCCCGATGGAGGCAGCAGAACTG GATGAGCAGCGTGAGAAGCTGGTGCTGTCGGCCGAGTGCCAGCTGGTGACGGTAGTGGCCGT GGTCCCAGGGCTGCTGGAGGTCACCACACAGAATGTATACTTCTACGATGGCAGCACTGAGC GCGTGGAAACCGAGGAGGGCATCGGCTATGATTTCCGGCGCCCACTGGCCCAGCTGCGTGAG GTCCACCTGCGGCGTTTCAACCTGCGCCGTTCAGCACTTGAGCTCTTCTTTATCGATCAGGC CAACTACTTCCTCAACTTCCCATGCAAGGTGGGCACGACCCCAGTCTCATCTCCTAGCCAGA CTCCGAGACCCCAGCCTGGCCCCATCCCACCCCATACCCAGGTACGGAACCAGGTGTACTCG TGGCTCCTGCGCCTACGGCCCCCCTCTCAAGGCTACCTAAGCAGCCGCTCCCCCAGGAGAT GCTGCGTGCCTCAGGCCTTACCCAGAAATGGGTACAGCGTGAGATATCCAACTTCGAGTACT TGATGCAACTCAACACCATTGCGGGGCGGACCTACAATGACCTGTCTCAGTACCCTGTGTTC CCCTGGGTCCTGCAGGACTACGTGTCCCCAACCCTGGACCTCAGCAACCCAGCCGTCTTCCG GGACCTGTCTAAGCCCATCGGTGTGGTGAACCCCAAGCATGCCCAGCTCGTGAGGGAGAAGT ATGAAAGCTTTGAGGACCCAGCAGGGACCATTGACAAGTTCCACTATGGCACCCACTACTCC AATGCAGCAGGCGTGATGCACTACCTCATCCGCGTGGAGCCCTTCACCTCCCTGCACGTCCA GCTGCAAAGTGGCCGCTTTGACTGCTCCGACCGGCAGTTCCACTCGGTGGCGCAGCCTGGC AGGCACGCCTGGAGAGCCCTGCCGATGTGAAGGAGCTCATCCCGGAATTCTTCTACTTTCCT GACTTCCTGGAGAACCAGAACGGTTTTGACCTGGGCTGTCTCCAGCTGACCAACGAGAAGGT AGGCGATGTGGTGCTACCCCCGTGGGCCAGCTCTCCTGAGGACTTCATCCAGCAGCACCGCC AGGCTCTGGAGTCGGAGTATGTGTCTGCACACCTACACGAGTGGATCGACCTCATCTTTGGC TACAAGCAGCGGGGGCCAGCCGCGAGGAGGCCCTCAATGTCTTCTATTACTGCACCTATGA GGGGGCTGTAGACCTGGACCATGTGACAGATGAGCGGGAACGGAAGGCTCTGGAGGGCATTA TCAGCAACTTTGGGCAGACTCCCTGTCAGCTGCTGAAGGAGCCACATCCAACTCGGCTCTCA GCTGAGGAAGCAGCCCATCGCCTTGCACGCCTGGACACTAACTCACCTAGCATCTTCCAGCA CCTGGACGAACTCAAGGCATTCTTCGCAGAGGTGACTGTGAGTGCCAGTGGGCTGCTGGGCA CCCACAGCTGGTTGCCCTATGACCGCAACATAAGCAACTACTTCAGCTTCAGCAAAGACCCC ACCATGGGCAGCCACAAGACGCAGCGACTGCTGAGTGGCCCGTGGGTGCCAGGCAGTGGTGT GAGTGGACAAGCACTGGCAGTGGCCCCGGATGGAAAGCTGCTATTCAGCGGTGGCCACTGGG ATGGCAGCCTGCGGGTGACTGCACTACCCCGTGGCAAGCTGTTGAGCCAGCTCAGCTGCCAC CTTGATGTAGTAACCTGCCTTGCACTGGACACCTGTGGCATCTACCTCATCTCAGGCTCCCG GGACACCACGTGCATGGTGTGGCGGCTCCTGCATCAGGGTGGTCTGTCAGTAGGCCTGGCAC CAAAGCCTGTGCAGGTCCTGTATGGGCATGGGGCTGCAGTGAGCTGTGTGGCCATCAGCACT GAACTTGACATGGCTGTCTGGATCTGAGGATGGAACTGTGATCATACACACTGTACGCCG CGGACAGTTTGTAGCGGCACTACGGCCTCTGGGTGCCACATTCCCTGGACCTATTTTCCACC TGGCATTGGGGTCCGAAGGCCAGATTGTGGTACAGAGCTCAGCGTGGGAACGTCCTGGGGCC CAGGTCACCTACTCCTTGCACCTGTATTCAGTCAATGGGAAGTTGCGGGCTTCACTGCCCCT GGCAGAGCAGCCTACAGCCCTGACGGTGACAGAGGACTTTGTGTTGCTGGGCACCGCCCAGT GCGCCCTGCACATCCTCCAACTAAACACACTGCTCCCGGCCGCGCCTCCCTTGCCCATGAAG GTGGCCATCCGCAGCGTGGCCGTGACCAAGGAGCGCAGCCACGTGCTGGTGGGCCTGGAGGA TGGCAAGCTCATCGTGGTGGTCGCGGGGCAGCCCTCTGAGGTGCGCAGCAGCCAGTTCGCGC GGAAGCTGTGGCGGTCCTCGCGGCGCATCTCCCAGGTGTCCTCGGGAGAGACGGAATACAAC $\tt CCTACTGAGGCGCGC\underline{TGA} ACCTGGCCAGTCCGGCTGCTCGGGCCCCGGCCCCGGCAGGCCTG$ GCCCGGGAGGCCCCAGAAGTCGGCGGGAACACCCCCGGGGTGGGCAGCCCAGGGGGTGA GCGGGGCCCACCCTGCCCAGCTCAGGGATTGGCGGGCGATGTTACCCCCTCAGGGATTGGCG GGCGGAAGTCCCGCCCTCGCCGGCTGAGGGGCCGCCCTGAGGGCCAGCACTGGCGTCT

FIGURE 23

MSOFEMDTYAKSHDLMSGFWNACYDMLMSSGORROWERAOSRRAFOELVLEPAORRARLEGL RYTAVLKOOATOHSMALLHWGALWRQLASPCGAWALRDTPIPRWKLSSAETYSRMRLKLVPN HHFDPHLEASALRDNLGEVPLTPTEEASLPLAVTKEAKVSTPPELLOEDOLGEDELAELETP MEAAELDEOREKLVLSAECOLVTVVAVVPGLLEVTTONVYFYDGSTERVETEEGIGYDFRRP LAOLREVHLRRFNLRRSALELFFIDQANYFLNFPCKVGTTPVSSPSQTPRPQPGPIPPHTQV RNOVYSWLLRLRPPSQGYLSSRSPQEMLRASGLTQKWVQREISNFEYLMOLNTIAGRTYNDL SOYPVFPWVLODYVSPTLDLSNPAVFRDLSKPIGVVNPKHAOLVREKYESFEDPAGTIDKFH YGTHYSNAAGVMHYLIRVEPFTSLHVQLQSGRFDCSDRQFHSVAAAWQARLESPADVKELIP EFFYFPDFLENQNGFDLGCLQLTNEKVGDVVLPPWASSPEDFIQQHRQALESEYVSAHLHEW IDLIFGYKORGPAAEEALNVFYYCTYEGAVDLDHVTDERERKALEGIISNFGQTPCQLLKEP HPTRLSAEEAAHRLARLDTNSPSIFOHLDELKAFFAEVTVSASGLLGTHSWLPYDRNISNYF SFSKDPTMGSHKTQRLLSGPWVPGSGVSGQALAVAPDGKLLFSGGHWDGSLRVTALPRGKLL SOLSCHLDVVTCLALDTCGIYLISGSRDTTCMVWRLLHQGGLSVGLAPKPVQVLYGHGAAVS CVAISTELDMAVSGSEDGTVIIHTVRRGQFVAALRPLGATFPGPIFHLALGSEGQIVVQSSA WERPGAQVTYSLHLYSVNGKLRASLPLAEQPTALTVTEDFVLLGTAOCALHILOLNTLLPAA PPLPMKVAIRSVAVTKERSHVLVGLEDGKLIVVVAGOPSEVRSSOFARKLWRSSRRISOVSS GETEYNPTEAR

FIGURE 24

CACGGCCCACCTTGTGAACTCCTCGTGCCCAGGGCTGATGTGCGTCTTCCAGGGCTACTCAT CCAAAGGCCTAATCCAACGTTCTGTCTTCAATCTGCAAATCTATGGGGTCCTGGGGCTCTTC TGGACCCTTAACTGGGTACTGGCCCTGGGCCAATGCGTCCTCGCTGGAGCCTTTGCCTCCTT CTACTGGGCCTTCCACAAGCCCCAGGACATCCCTACCTTCCCCTTAATCTCTGCCTTCATCC GCACACTCCGTTACCACACTGGGTCATTGGCATTTGGAGCCCTCATCCTGACCCTTGTGCAG ATAGCCCGGGTCATCTTGGAGTATATTGACCACAAGCTCAGAGGAGTGCAGAACCCTGTAGC CCGCTGCATCATGTGCTGTTTCAAGTGCTGCCTCTGGTGTCTGGAAAAATTTATCAAGTTCC TAAACCGCAATGCATACATCATGATCGCCATCTACGGGAAGAATTTCTGTGTCTCAGCCAAA **AATGCGTTCATGCTACTCATGCGAAACATTGTCAGGGTGGTCGTCCTGGACAAAGTCACAGA** CCTGCTGCTGTTCTTTGGGAAGCTGCTGGTGGTCGGAGGCGTGGGGGGTCCTGTCTTTT TTTTCTCCGGTCGCATCCCGGGGCTGGGTAAAGACTTTAAGAGCCCCCACCTCAACTATTAC TGGCTGCCCATCATGACCTCCATCCTGGGGGCCTATGTCATCGCCAGCGGCTTCTTCAGCGT TTTCGGCATGTGTGTGGACACGCTCTTCCTCTGCTTCCTGGAAGACCTGGAGCGGAACAACG GCTCCCTGGACCGGCCCTACTACATGTCCAAGAGCCTTCTAAAGATTCTGGGCAAGAAGAAC GAGGCGCCCCGGACAACAAGAAGAGGAAGAAG<u>TGA</u>CAGCTCCGGCCCTGATCCAGGACTGC ACCCCACCCCACCGTCCAGCCATCCAACCTCACTTCGCCTTACAGGTCTCCATTTTGTGGT AAAAAAAGGTTTTAGGCCAGGCGCCGTGGCTCACGCCTGTAATCCAACACTTTGAGAGGCTG AGGCGGGCGGATCACCTGAGTCAGGAGTTCGAGACCAGCCTGGCCAACATGGTGAAACCTCC GTCTCTATTAAAAATACAAAAATTAGCCGAGAGTGGTGGCATGCACCTGTCATCCCAGCTAC TCGGGAGGCTGAGGCAGGAGATCGCTTGAACCCGGGAGGCAGAGGTTGCAGTGAGCCGAGA AAAGATTTTATTAAAGATATTTTGTTAACTC

FIGURE 25

RTRGRTRGGCEKVPINTSCNPTAHLVNSSCPGLMCVFQGYSSKGLIQRSVFNLQIYGVLGLF
WTLNWVLALGQCVLAGAFASFYWAFHKPQDIPTFPLISAFIRTLRYHTGSLAFGALILTLVQ
IARVILEYIDHKLRGVQNPVARCIMCCFKCCLWCLEKFIKFLNRNAYIMIAIYGKNFCVSAK
NAFMLLMRNIVRVVVLDKVTDLLLFFGKLLVVGGVGVLSFFFFSGRIPGLGKDFKSPHLNYY
WLPIMTSILGAYVIASGFFSVFGMCVDTLFLCFLEDLERNNGSLDRPYYMSKSLLKILGKKN
EAPPDNKKRKK

FIGURE 26

GAGTCTTGACCGCCGCCGGGCTCTTGGTACCTCAGCGCGAGCGCCAGGCGTCCGGCCGCCGT GGCT<u>ATG</u>TTCGTGTCCGATTTCCGCAAAGAGTTCTACGAGGTGGTCCAGAGCCAGAGGGTCC CAGTGTGACCACGTGCAATATACGCTGGTTCCAGTTTCTGGGTGGCAAGAACTTGAAACTGC ATTTCTTGAGCATAAAGAACAGTTTCATTATTTTATTCTCATAAACTGTGGAGCTAATGTAG CCAGTCAATGTCGTCAATGTATACAACGATACCCAGATCAAATTACTCATTAAACAAGATGA TGACCTTGAAGTTCCCGCCTATGAAGACATCTTCAGGGATGAAGAGGAGGATGAAGAGCATT CAGGAAATGACAGTGATGGGTCAGAGCCTTCTGAGAAGCGCACACGGTTAGAAGAGGAGATA CTTTGACTACGAGCAGTATGAATATCATGGGACATCGTCAGCCATGGTGATGTTTGAGCTGG CTTGGATGCTGTCCAAGGACCTGAATGACATGCTGTGGTGGGCCATCGTTGGACTAACAGAC CAGTGGGTGCAAGACAAGATCACTCAAATGAAATACGTGACTGATGTTGGTGTCCTGCAGCG CCACGTTTCCCGCCACAACCACCGGAACGAGGATGAGGAGAACACACTCTCCGTGGACTGCA CACGGATCTCCTTTGAGTATGACCTCCGCCTGGTGCTCTACCAGCACTGGTCCCTCCATGAC AGCCTGTGCAACACCAGCTATACCGCAGCCAGGTTCAAGCTGTGGTCTGTGCATGGACAGAA GCGGCTCCAGGAGTTCCTTGCAGACATGGGTCTTCCCCTGAAGCAGGTGAAGCAGAAGTTCC AGGCCATGGACATCTCCTTGAAGGAGAATTTGCGGGAAATGATTGAAGAGTCTGCAAATAAA TCTGGCCAGCGACGTGGTCTTTGCCACCATGTCTTTGATGGAGAGCCCCGAGAAGGATGGCT CAGGGACAGATCACTTCATCCAGGCTCTGGACAGCCTCTCCAGGAGTAACCTGGACAAGCTG TACCATGGCCTGGAACTCGCCAAGAAGCAGCTGCGAGCCACCCAGCAGACCATTGCCAGCTGC ${\tt CTTTGCACCAACCTCGTCATCTCCCAGGGGCCTTTCCTGTACTGCTCTCTCATGGAGGGCAC}$ TCCAGATGTCATGCTGTTCTCTAGGCCGGCATCCCTAAGCCTGCTCAGCAAACACCTGCTCA AGTCCTTTGTGTGTTCGACAAAGAACCGGCGCTGCAAACTGCTGCCCCTGGTGATGGCTGCC CCCCTGAGCATGGAGCATGGCACAGTGACCGTGGTGGGCATCCCCCCAGAGACCGACAGCTC GGACAGGAAGAACTTTTTTGGGAGGGCGTTTGAGAAGGCAGCGGAAAGCACCAGCTCCCGGA TGCTGCACAACCATTTTGACCTCTCAGTAATTGAGCTGAAAGCTGAGGATCGGAGCAAGTTT ${\tt CTGGACGCACTTATTTCCCTCCTGTCC} \underline{{\tt TAG}} \underline{{\tt GAATTTGATTCTTCCAGAATGACCTTCTTATT}$ TATGTAACTGGCTTTCATTTAGATTGTAAGTTATGGACATGATTTGAGATGTAGAAGCCATT TTTTATTAAATAAAATGCTTATTTTAGGAAA

FIGURE 27

MFVSDFRKEFYEVVQSQRVLLFVASDVDALCACKILQALFQCDHVQYTLVPVSGWQELETAF

LEHKEQFHYFILINCGANVDLLDILQPDEDTIFFVCDSHRPVNVVNVYNDTQIKLLIKQDDD

LEVPAYEDIFRDEEEDEEHSGNDSDGSEPSEKRTRLEEEIVEQTMRRRQRREWEARRRDILF

DYEQYEYHGTSSAMVMFELAWMLSKDLNDMLWWAIVGLTDQWVQDKITQMKYVTDVGVLQRH

VSRHNHRNEDEENTLSVDCTRISFEYDLRLVLYQHWSLHDSLCNTSYTAARFKLWSVHGQKR

LQEFLADMGLPLKQVKQKFQAMDISLKENLREMIEESANKFGMKDMRVQTFSIHFGFKHKFL

ASDVVFATMSLMESPEKDGSGTDHFIQALDSLSRSNLDKLYHGLELAKKQLRATQQTIASCL

CTNLVISQGPFLYCSLMEGTPDVMLFSRPASLSLLSKHLLKSFVCSTKNRRCKLLPLVMAAP

LSMEHGTVTVVGIPPETDSSDRKNFFGRAFEKAAESTSSRMLHNHFDLSVIELKAEDRSKFL

DALISLLS

FIGURE 28

WO 99/63088

29/3-10

FIGURE 29

CAGGAACCCTCTCTTTGGGTCTGGATTGGGACCCCTTTCCAGTACCATTTTTTCTAGTGAAC CACGAAGGGACGATACCAGAAAACACCCTCAACCCAAAGGAAATAGACTACAGCCCCAATTG GTCTTCCCTTTATCGAGTCAAGAAACCCCCCCTTCTTGAGCTATTTACAGCTTTTAACAATT GAGTAAAGTACGCTCCGGTCACC<u>ATG</u>GTGACAGCCGCCCTGGGTCCCGTCTGGGCAGCGCTC CTGCTCTTTCTCCTGATGTGTGAGATCCGTATGGTGGAGCTCACCTTTGACAGAGCTGTGGC CAGCGGCTGCCAACGGTGCTGTGACTCTGAGGACCCCCTGGATCCTGCCCATGTATCCTCAG CCTCTTCCTCCGGCCGCCCCCACGCCCTGCCTGAGATCAGACCCTACATTAATATCACCATC TCCCCAAGGGGAGCCTGGCCCTCAGGGCAGCAAGGGTGACAAGGGGGAGATGGGCAGCCCCG GCGCCCGTGCCAGAAGCGCTTCTTCGCCTTCTCAGTGGGCCGCAAGACGGCCCTGCACAGC GGCGAGGACTTCCAGACGCTGCTCTTCGAAAGGGTCTTTGTGAACCTTGATGGGTGCTTTGA CATGGCGACCGGCCAGTTTGCTGCTCCCCTGCGTGGCATCTACTTCTTCAGCCTCAATGTGC ACAGCTGGAATTACAAGGAGACGTACGTGCACATTATGCATAACCAGAAAGAGGCTGTCATC CTGTACGCGCAGCCAGCGAGCGCAGCATCATGCAGAGCCAGAGTGTGATGCTGGACCTGGC CTACGGGGACCGCGTCTGGGTGCGGCTCTTCAAGCGCCAGCGCGAGAACGCCATCTACAGCA ACGACTTCGACACCTACATCACCTTCAGCGGCCACCTCATCAAGGCCGAGGACGAC<u>TGA</u>GGG CCTCTGGGCCACCCTCCCGGCTGGAGAGCTCAGGTGCTGGTCCCGTCCCCTGCAGGGCTCAG TTTGCACTGCTGTGAAGCAGGAAGGCCAGGGAGGTCCCCGGGGACCTGGCATTCTGGGGAGA TGGACCTATTTTAAGAAGCTTGCTAACCTAAATATTCTAGAACTTTCCCAGCCTCGTAGCCC AGCACTTCTCAAACTTGGAAATGCATGCGAATCACCCGGGGTTCGTGTTAAATGCAGATTCT GACTCAGCAGGTCTGAGTGGGTCCAGGATTCTGTGTTTCTCATATGTTCCTGGGTGATGCTG ATGGGGTCAGTCTATGAACCACACTGGAGCAACCAGGTTCTAGGACTTTCTCAATATTCTAG TGAGACAGAGTCTTGCTCTGTTGCCCAGGCTAGAGTGCAGTGGTGCAATCTCAGTTCACTGC AACCTCTGCCTCCCGGGTTCAAGCGATTCTTCTGCCTCAGCCTCCCTAGTGGCTGGGATTAC AGGCGCCTGCTACCATGCCTGGCTAATTTTTTGTATTTTTAGTAGAGATGGGGTTTCACCATA GCTGGGATTACAGGTGTGAGCCACCGTGCCTGGCCAATTCCAACATTCTTAAATTCTCTCAT CCCTCCAGGGCTCCCCGTGCTATGTTCTCTTTACCCCTTCCCCCTCTTCTCTTGCTCAGGCC GGGTCCCGGGAAGGGTGAGGGGGTCAGACACAGGCCCTGCCCTGCCCTCAGTGACTGGCCA GTCCAGCCCAGGCGGGGAGAGATGTGTACATAGGTTTTAAAGCAGACCCAGAGCTCATGGGG GCCTGTGTTCTGGGTGTTCAGGTGCTGCTGGTCCTCCATTACCCACTGCTCCCCAAGGCTGG TGGGACGGGGTCCCGGTGGCAGGGCAGGTATCTCCTTCCCGTTCCTCATCCACCTGCCCAG TGCTCATCGTTACAGCAAACCCCAGGGGGCCTTGGCCAGGTCAAGGGTTCTGTGAGGAGAGG ACCCAGGAGTGTGGGGGCATTTGGGGGGTGAAGTGGCCCCCGAAGAATGGAACCCACACCCA TAGCTCTCCCCACAGCTGATACGGCATCCTGCGAGAAGACCTGCCCTCCTCACTGGGATCCC CTTCCTGCCTCCCCAGGGCTCTGCCAGGGCCTTGCTCAGTCCCTTCCACCAAAGTCATCT CTCTGCCCCTCATGCCCCTCTCACCGGCCCAGTGCCCCGACTCTCCAGGCTTTATCAAGGTG CTAAGGCCCGGGTGGGCAGCTCCTCGTCTCAGAGCCCTCCTCCGGCCTGGTGCTGCCTTTAC AAACACCTGCAGGAGAAGGGCCACGGAAGCCCCAGGCTTTAGAGCCCTCAGCAGGTCTGGGG AGCTAGAGCAAAGGAGGGACCTCAGGCCTTCCGTTTCTTCTTCCAGGGTGGGGTGGCCTGGT CCATTGGTGCTCATGCAGACTCTGGGGCTGAGGTGCCCCGGGGGGGTGATCTCTGGTGCTCAC AGCCGAGGGAGCCGTGGCTCCATGGCCAGATGACGGAAACAGGGTCTGACCAAGTGCCAGGA

FIGURE 30

MVTAALGPVWAALLIFILMCEIRMVELTFDRAVASGCQRCCDSEDPLDPAHVSSASSSGRPH
ALPEIRPYINITILKGDKGDPGPMGLPGYMGREGPQGEPGPQGSKGDKGEMGSPGAPCQKRF
FAFSVGRKTALHSGEDFQTLLFERVFVNLDGCFDMATGQFAAPLRGIYFFSLNVHSWNYKET
YVHIMHNQKEAVILYAQPSERSIMQSQSVMLDLAYGDRVWVRLFKRQRENAIYSNDFDTYIT
FSGHLIKAEDD

Important features: Signal peptide: amino acids 1-20

N-glycosylation site.
amino acids 72-75

Clq domain proteins.
amino acids 144-178, 78-111 and 84-117

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ACTCGAACGCAGTTGCTTCGGGACCCAGGACCCCCTCGGGCCCGACCCGCCAGGAAAGACTG CTCCAGGGTCCCTCTGCTGCCGCCGCTGCTCCTGCTACTGGCCCTGGGGCCTGGGGTGCAGG GCTGCCCATCCGGCTGCCAGTGCAGCCAGCCACAGACAGTCTTCTGCACTGCCCGCCAGGGG ACCACGGTGCCCCGAGACGTGCCACCCGACACGGTGGGGCTGTACGTCTTTGAGAACGGCAT CACCATGCTCGACGCAGGCAGCTTTGCCGGCCTGCCGGGCCTGCAGCTCCTGGACCTGTCAC AGAACCAGATCGCCAGCCTGCCCAGCGGGGTCTTCCAGCCACTCGCCAACCTCAGCAACCTG GACCTGACGGCCAACAGGCTGCATGAAATCACCAATGAGACCTTCCGTGGCCTGCGGCGCCT CGAGCGCCTCTACCTGGGCAAGAACCGCATCCGCCACATCCAGCCTGGTGCCTTCGACACGC TCGACCGCCTCCTGGAGCTCAAGCTGCAGGACAACGAGCTGCGGGCACTGCCCCCGCTGCGC CTGCCCGCCTGCTGCTGCTGGACCTCAGCCACAACAGCCTCCTGGCCCTGGAGCCCGGCAT CCTGGACACTGCCAACGTGGAGGCGCTGCGGCTGGTCTGGGGCTGCAGCAGCTGGACG AGGGGCTCTTCAGCCGCTTGCGCAACCTCCACGACCTGGATGTGTCCGACAACCAGCTGGAG CGAGTGCCACCTGTGATCCGAGGCCTCCGGGGCCTGACGCCCTGCGGCTGGCCGGCAACAC TGAGCAACCTAAGCCTGCAGGCCCTGCCTGGCGACCTCTCGGGCCTCTTCCCCCGCCTGCGG CTGCTGGCAGCTGCCCGCAACCCCTTCAACTGCGTGTGCCCCCTGAGCTGGTTTGGCCCCCTG GGTGCGCGAGAGCCACGTCACACTGGCCAGCCCTGAGGAGACGCGCTGCCACTTCCCGCCCA AGAACGCTGGCCGGCTGCTCCTGGAGCTTGACTACGCCGACTTTGGCTGCCCAGCCACCACC ACCACAGCCACAGTGCCCACCACGAGGCCCGTGGTGCGGGAGCCCACAGCCTTGTCTTCTAG CTGCCCCACCGACTGTAGGGCCTGTCCCCCAGCCCCAGGACTGCCCACCGTCCACCTGCCTC AATGGGGGCACATGCCACCTGGGGACACGGCACCACCTGGCGTGCTTGTGCCCCGAAGGCTT CACGGGCCTGTACTGTGAGAGCCAGATGGGGCAGGGGACACGGCCCAGCCCTACACCAGTCA CGCCGAGGCCACCACGGTCCCTGACCCTGGGCATCGAGCCGGTGAGCCCCACCTCCCTGCGC GTGGGGCTGCAGCGCTACCTCCAGGGGAGCTCCGTGCAGCTCAGGAGCCTCCGTCTCACCTA AGTACACGGTCACCCAGCTGCGGCCCAACGCCACTTACTCCGTCTGTGTCATGCCTTTGGGG CCCGGGCGGGTGCCGGAGGGCGAGGGCCTGCGGGGAGGCCCATACACCCCCAGCCGTCCA CTCCAACCACGCCCCAGTCACCCAGGCCCGCGAGGGCAACCTGCCGCTCCTCATTGCGCCCG CCCTGGCCGCGGTGCTCCTGGCCGCGCTGGCTGCGGTGGGGGCAGCCTACTGTGTGCGGCGG GGGCGGCCATGGCAGCAGCGGCTCAGGACAAAGGGCAGGTGGGGCCAGGGGCTGGGCCCCT GGAA CTGGAGGGAGTGAAGGTCCCCTTGGAGCCAGGCCCGAAGGCAACAGAGGCGGTGGAG AGGCCCTGCCCAGCGGGTCTGAGTGTGAGGTGCCACTCATGGGCTTCCCAGGGCCTGGCCTC GGCTCTCAGCCAGTGAGATGGCCAGCCCCCTCCTGCTGCCACACCACGTAAGTTCTCAGTCC CAACCTCGGGGATGTGTGCAGACAGGGCTGTGTGACCACAGCTGGGCCCTGTTCCCTCTGGA CCTCGGTCTCCTCATCTGTGAGATGCTGTGGCCCAGCTGACGAGCCCTAACGTCCCCAGAAC CGAGTGCCTATGAGGACAGTGTCCGCCCTGCCCTCCGCAACGTGCAGTCCCTGGGCACGGCG GGCCTGCCATGTGCTGGTAACGCATGCCTGGGTCCTGCTGGGCTCTCCCACTCCAGGCGGA CCCTGGGGGCCAGTGAAGGAAGCTCCCGGAAAGAGCAGAGGGAGAGCGGGTAGGCGGCTGTG TGACTCTAGTCTTGGCCCCAGGAAGCGAAGGAACAAAAGAAACTGGAAAGGAAGATGCTTTA GGAACATGTTTTGCTTTTTAAAATATATATATATATATAAGAGATCCTTTCCCATTTATTCTG GGAAGATGTTTTCAAACTCAGAGACAAGGACTTTGGTTTTTGTAAGACAAACGATGATATG AAGGCCTTTTGTAAGAAAAAATAAAAGATGAAGTGTGAAA

FIGURE 32

MCSRVPLLLPLLLLALGPGVQGCPSGCQCSQPQTVFCTARQGTTVPRDVPPDTVGLYVFEN
GITMLDAGSFAGLPGLQLLDLSQNQIASLPSGVFQPLANLSNLDLTANRLHEITNETFRGLR
RLERLYLGKNRIRHIQPGAFDTLDRLLELKLQDNELRALPPLRLPRLLLLDLSHNSLLALEP
GILDTANVEALRLAGLGLQQLDEGLFSRLRNLHDLDVSDNQLERVPPVIRGLRGLTRLRLAG
NTRIAQLRPEDLAGLAALQELDVSNLSLQALPGDLSGLFPRLRLLAAARNPFNCVCPLSWFG
PWVRESHVTLASPEETRCHFPPKNAGRLLLELDYADFGCPATTTTATVPTTRPVVREPTALS
SSLAPTWLSPTAPATEAPSPPSTAPPTVGPVPQPQDCPPSTCLNGGTCHLGTRHHLACLCPE
GFTGLYCESQMGQGTRPSPTPVTPRPPRSLTLGIEPVSPTSLRVGLQRYLQGSSVQLRSLRL
TYRNLSGPDKRLVTLRLPASLAEYTVTQLRPNATYSVCVMPLGPGRVPEGEEACGEAHTPPA
VHSNHAPVTQAREGNLPLLIAPALAAVLLAALAAVGAAYCVRRGRAMAAAAQDKGQVGPGAG
PLELEGVKVPLEPGPKATEGGGEALPSGSECEVPLMGFPGPGLQSPLHAKPYI

73/3\0 FIGURE 33

GAATCATCCACGCACCTGCAGCTCTGCTGAGAGAGTGCAAGCCGTGGGGGTTTTGAGCTCAT CTTCATCATTCATATGAGGAAATAAGTGGTAAAATCCTTGGAAATACAATGAGACTCATCAG AAACATTTACATATTTTGTAGTATTGTTATGACAGCAGAGGGTGATGCTCCAGAGCTGCCAG AAGAAAGGAACTGATGACCAACTGCTCCAACATGTCTCTAAGAAAGGTTCCCGCAGACTTG ACCCCAGCCACAACGACACTGGATTTATCCTATAACCTCCTTTTTCAACTCCAGAGTTCAGA TTTTCATTCTGTCTCCAAACTGAGAGTTTTGATTCTATGCCATAACAGAATTCAACAGCTGG ATCTCAAAACCTTTGAATTCAACAAGGAGTTAAGATATTTAGATTTGTCTAATAACAGACTG TGACACCATGCCTATCTGTGAGGAAGCTGGCAACATGTCACACCTGGAAATCCTAGGTTTGA GTGGGGCAAAAATACAAAAATCAGATTTCCAGAAAATTGCTCATCTGCATCTAAATACTGTC TTCTTAGGATTCAGAACTCTTCCTCATTATGAAGAAGGTAGCCTGCCCATCTTAAACACAAC AAAACTGCACATTGTTTTACCAATGGACACAAATTTCTGGGTTCTTTTGCGTGATGGAATCA AGACTTCAAAAATATTAGAAATGACAAAATATAGATGGCAAAAGCCAATTTGTAAGTTATGAA ATGCAACGAAATCTTAGTTTAGAAAATGCTAAGACATCGGTTCTATTGCTTAATAAAGTTGA TTCAGATCCGAAATGTGACTTTTGGTGGTAAGGCTTATCTTGACCACAATTCATTTGACTAC TCAAATACTGTAATGAGAACTATAAAATTGGAGCATGTACATTTCAGAGTGTTTTACATTCA **ACAGGATAAAATCTATTTGCTTTTGACCAAAATGGACATAGAAAACCTGACAATATCAAATG** CACAAATGCCACACATGCTTTTCCCGAATTATCCTACGAAATTCCAATATTTAAATTTTGCC **AATAATATCTTAACAGACGAGTTGTTTAAAAGAACTATCCAACTGCCTCACTTGAAAACTCT** CATTTTGAATGGCAATAAACTGGAGACACTTTCTTTAGTAAGTTGCTTTGCTAACAACACAC CCTTGGAACACTTGGATCTGAGTCAAAATCTATTACAACATAAAAATGATGAAAATTGCTCA TGGCCAGAAACTGTGGTCAATATGAATCTGTCATACAATAAATTGTCTGATTCTGTCTTCAG GTGCTTGCCCAAAAGTATTCAAATACTTGACCTAAATAATAACCAAATCCAAACTGTACCTA AAGAGACTATTCATCTGATGGCCTTACGAGAACTAAATATTGCATTTAATTTTCTAACTGAT CTCCCTGGATGCAGTCATTTCAGTAGACTTCAGTTCTGAACATTGAAATGAACTTCATTCT CAGCCCATCTCTGGATTTTGTTCAGAGCTGCCAGGAAGTTAAAACTCTAAATGCGGGAAGAA ATGATGGTTGGATGGTCAGATTCATACACCTGTGAATACCCTTTAAACCTAAGGGGAACTAG GTTAAAAGACGTTCATCTCCACGAATTATCTTGCAACAGCTCTGTTGATTGTCACCATTG TGGTTATTATGCTAGTTCTGGGGTTGGCTGTGGCCTTCTGCTGTCTCCACTTTGATCTGCCC TGGTATCTCAGGATGCTAGGTCAATGCACACAAACATGG<u>CACAGGGTTAGGAAAACAACCCA</u> CTTTATGAAAGCTACTTTGACCCTGGCAAAAGCATTAGTGAAAATATTGTAAGCTTCATTGA GAAAAGCTATAAGTCCATCTTTGTTTTGTCTCCCAACTTTGTCCAGAATGAGTGGTGCCATT ATGAATTCTACTTTGCCCACCACAATCTCTTCCATGAAAATTCTGATCATAAATTCTTATC TTACTGGAACCCATTCCATTCTATTGCATTCCCACCAGGTATCATAAACTGAAAGCTCTCCT GGAAAAAAAAGCATACTTGGAATGGCCCAAGGATAGGCGTAAATGTGGGCTTTTCTGGGCAA ACCTTCGAGCTGCTATTAATGTTAATGTATTAGCCACCAGAGAAATGTATGAACTGCAGACA TTCACAGAGTTAAATGAAGAGTCTCGAGGTTCTACAATCTCTCTGATGAGAACAGATTGTCT ATAAAATCCCACAGTCCTTGGGAAGTTGGGGACCACATACACTGTTGGGATGTACATTGATA CAACCTTTATGATGGCAATTTGACAATATTTATTAAAATAAAAAATGGTTATTCCCTTCATA TCAGTTTCTAGAAGGATTTCTAAGAATGTATCCTATAGAAACACCTTCACAAGTTTATAAGG GCTTATGGAAAAAGGTGTTCATCCCAGGATTGTTTATAATCATGAAAAATGTGGCCAGGTGC GAGATGGAGACCATCCTGGCCAACATGGTGAAACCCTGTCTCTACTAAAAATACAAAAATTA GCTGGGCGTGATGGTGCACGCCTGTAGTCCCAGCTACTTGGGAGGCTGAGGCAGGAGAATCG CTTGAACCCGGGAGGTGGCAGTTGCAGTGAGCTGAGATCGAGCCACTGCACTCCAGCCTGGT TCATGGCCACAAAATAAGGTCTAATTCAATAAATTATAGTACATTAATGTAATATAATATTA CATGCCACTAAAAAGAATAAGGTAGCTGTATATTTCCTGGTATGGAAAAAACATATTAATAT GTTATAAACTATTAGGTTGGTGCAAAACTAATTGTGGTTTTTTGCCATTGAAATGGCATTGAA ATAAAAGTGTAAAGAAATCTATACCAGATGTAGTAACAGTGGTTTGGGTCTGGGAGGTTTGGA TTACAGGGAGCATTTGATTTCTATGTTGTGTATTTCTATAATGTTTGAATTGTTTAGAATGA ATCTGTATTTCTTTTATAAGTAGAAAAAAAAAAAAAAGATAGTTTTTACAGCCT

34/3-10 · FIGURE 34

MRLIRNIYIFCSIVMTAEGDAPELPEERELMTNCSNMSLRKVPADLTPATTTLDLSYNLLFQ
LQSSDFHSVSKLRVLILCHNRIQQLDLKTFEFNKELRYLDLSNNRLKSVTWYLLAGLRYLDL
SFNDFDTMPICEEAGNMSHLEILGLSGAKIQKSDFQKIAHLHLNTVFLGFRTLPHYEEGSLP
ILNTTKLHIVLPMDTNFWVLLRDGIKTSKILEMTNIDGKSQFVSYEMQRNLSLENAKTSVLL
LNKVDLLWDDLFLILQFVWHTSVEHFQIRNVTFGGKAYLDHNSFDYSNTVMRTIKLEHVHFR
VFYIQQDKIYLLLTKMDIENLTISNAQMPHMLFPNYPTKFQYLNFANNILTDELFKRTIQLP
HLKTLILNGNKLETLSLVSCFANNTPLEHLDLSQNLLQHKNDENCSWPETVVNMNLSYNKLS
DSVFRCLPKSIQILDLNNNQIQTVPKETIHLMALRELNIAFNFLTDLPGCSHFSRLSVLNIE
MNFILSPSLDFVQSCQEVKTLNAGRNPFRCTCELKNFIQLETYSEVMMVGWSDSYTCEYPLN
LRGTRLKDVHLHELSCNTALLIVTIVVIMLVLGLAVAFCCLHFDLPWYLRMLGQCTQTWHRV
RKTTQEQLKRNVRFHAFISYSEHDSLWVKNELIPNLEKEDGSILICLYESYFDPGKSISENI
VSFIEKSYKSIFVLSPNFVQNEWCHYEFYFAHHNLFHENSDHIILILLEPIPFYCIPTRYHK
LKALLEKKAYLEWPKDRRKCGLFWANLRAAINVNVLATREMYELQTFTELNEESRGSTISLM

ろ5/310 **FIGURE 35A**

GGGGCTTTCTTGGGCTTGGCTGCTTGGAACACCTGCCTCCAAGGACCGGCCTCGGAGGGGT CTGCGCGCCCTGTCCGCCCCGGCCCAGCCCAGCCCGGGGCCGGTCACACGCGCA GCCAGCCGCCGCCCCCGCGCCCAAGCGCGCCCTCTGCTGCGCCCTTGCCCCCG CGCCAGCTTCTGCGCCCGCAGCCCGCCCGGCGCCCCCGGTGACCGTGACCCTGCCCTGGGCG CGGGGCGGAGCAGGCATGTCCCGCCCGGGGACCGCTACCCCAGCGCTGGCCCTGGTGCTCCT GGCAGTGACCCTGGCCGGGGTCGGAGCCCAGGGCGCAGCCCTCGAGGACCCTGATTATTACG GGCAGGAGATCTGGAGCCGGGAGCCCTACTACGCGCGCCCGGAGCCCGAGCTCGAGACCTTC GCCCAAGAGGCCACCAAGCCCAAGAAAGCTCCCAAGAGGGAAAGTCGGCTCCGGAGCCGC CTCCACCAGGTAAACACAGCAACAAAAAGTTATGAGAACCAAGAGCTCTGAGAAGGCTGCC TCTGGAAACCTTAAAAATCACAGACTTCCAGCTCCATGCCTCCACGGTGAAGCGCTATGGCC TGGGGGCACATCGAGGGAGACTCAACATCCAGGCGGCATTAATGAAAATGATTTTTATGAC GGAGCGTGGTGCGCGGGAAGAATGACCTCCAGCAGTGGATTGAAGTGGATGCTCGGCGCCT GACCAGATTCACTGGTGTCATCACTCAAGGGAGGAACTCCCTCTGGCTGAGTGACTGGGTGA CATCCTATAAGGTCATGGTGAGCAATGACAGCCACACGTGGGTCACTGTTAAGAATGGATCT GGAGACATGATATTTGAGGGAAACAGTGAGAAGGAGATCCCTGTTCTCAATGAGCTACCCGT CCCCATGGTGGCCCGCTACATCCGCATAAACCCTCAGTCCTGGTTTGATAATGGGAGCATCT GCATGAGAATGGAGATCCTGGGCTGCCCACTGCCAGATCCTAATAATTATTATCACCGCCGG AACGAGATGACCACCACTGATGACCTGGATTTTAAGCACCACAATTATAAGGAAATGCGCCA GTTGATGAAAGTTGTGAATGAAATGTCCCCAATATCACCAGAATTTACAACATTGGAAAAA GCCACCAGGGCCTGAAGCTGTATGCTGTGGAGATCTCAGATCACCCTGGGGAGCATGAAGTC GGTGAGCCCGAGTTCCACTACATCGCGGGGCCCACGGCAATGAGGTGCTGGGCCGGGAGCT GCTGCTGCTGGTGCAGTTCGTGTGTCAGGAGTACTTGGCCCGGAATGCGCGCATCGTCC GCCTACGAAGGGGGCTCGGAGCTGGGAGGCTGGTCCCTGGGACGCTGGACCCACGATGGAAT TGACATCAACAACAACTTTCCTGATTTAAACACGCTGCTCTGGGAGGCAGAGGATCGACAGA ATGTCCCCAGGAAAGTTCCCAATCACTATATTGCAATCCCTGAGTGGTTTCTGTCGGAAAAT GGGCGCAACCTGCAGGGCGGCGAGCTGGTGGTGGCGTATCCCTACGACCTGGTGCGGTCCC TCCTATGCCTCCACACCCCCCTCATGACAGACGCCCGGAGGAGGGTGTGCCACACGGAGGA CTTCCAGAAGGAGGAGGCACTGTCAATGGGGCCTCCTGGCACACCGTCGCTGGAAGTCTGA ACGATTTCAGCTACCTTCATACAAACTGCTTCGAACTGTCCATCTACGTGGGCTGTGATAAA TACCCACATGAGAGCCAGCTGCCCGAGGAGTGGGAGAATAACCGGGAATCTCTGATCGTGTT CATGGAGCAGGTTCATCGTGGCATTAAAGGCTTGGTGAGAGATTCACATGGAAAAGGAATCC CAAACGCCATTATCTCCGTAGAAGGCATTAACCATGACATCCGAACAGCCAACGATGGGGAT TACTGGCGCCTCCTGAACCCTGGAGAGTATGTGGTCACAGCAAAGGCCGAAGGTTTCACTGC **ATCCACCAAGAACTGTATGGTTGGCTATGACATGGGGGCCACAAGGTGTGACTTCACACTTA** GCAAAACCAACATGGCCAGGATCCGAGAGATCATGGAGAAGTTTGGGAAGCAGCCCGTCAGC CTGCCAGCCAGGCGGTGAAGCTGCGGGGGGGGGAAGAGACACCGTGGG<u>TGA</u>CCCTCCTG GACTCACTCACTGTTTTCCTCTGTAATTCAAGAAGTGCCTGGAAGAGAGGGTGCATTGTG TCCAAATAACTTGGACAGAGCAGCAGAGAAAAGCTGATGGGAGTGAGAGAACTCAGCAAGCC AACCTGGGAATCAGAGAGAGAAGGAGGAGGGGGGGGCCTGTCCGTTCAGAGCCTCTGGCTGC

36/340 FIGURE 35B

3ギ/3い **FIGURE 36**

MSRPGTATPALALVLLAVTLAGVGAQGAALEDPDYYGQEIWSREPYYARPEPELETFSPPLP
AGPGEEWERRPQEPRPPKRATKPKKAPKREKSAPEPPPPGKHSNKKVMRTKSSEKAANDDHS
VRVAREDVRESCPPLGLETLKITDFQLHASTVKRYGLGAHRGRLNIQAGINENDFYDGAWCA
GRNDLQQWIEVDARRLTRFTGVITQGRNSLWLSDWVTSYKVMVSNDSHTWVTVKNGSGDMIF
EGNSEKEIPVLNELPVPMVARYIRINPQSWFDNGSICMRMEILGCPLPDPNNYYHRRNEMTT
TDDLDFKHHNYKEMRQLMKVVNEMCPNITRIYNIGKSHQGLKLYAVEISDHPGEHEVGEPEF
HYIAGAHGNEVLGRELLLLLVQFVCQEYLARNARIVHLVEETRIHVLPSLNPDGYEKAYEGG
SELGGWSLGRWTHDGIDINNNFPDLNTLLWEAEDRQNVPRKVPNHYIAIPEWFLSENATVAA
ETRAVIAWMEKIPFVLGGNLQGGELVVAYPYDLVRSPWKTQEHTPTPDDHVFRWLAYSYAST
HRLMTDARRRVCHTEDFQKEEGTVNGASWHTVAGSLNDFSYLHTNCFELSIYVGCDKYPHES
QLPEEWENNRESLIVFMEQVHRGIKGLVRDSHGKGIPNAIISVEGINHDIRTANDGDYWRLL
NPGEYVVTAKAEGFTASTKNCMVGYDMGATRCDFTLSKTNMARIREIMEKFGKQPVSLPARR
LKLRGRKRRQRG

38 /310 **FIGURE 37**

CTAAGAGGACAAGATGAGGCCCGGCCTCTCATTTCTCCTAGCCCTTCTGTTCTTCCTTGGCC AAGCTGCAGGGGATTTGGGGGATGTGGGACCTCCAATTCCCAGCCCCGGCTTCAGCTCTTTC CCAGGTGTTGACTCCAGCTCCAGCTTCAGCTCCAGCTCCAGGTCGGGCTCCAGCTCCAGCCG CAGCTTAGGCAGCGGAGGTTCTGTGTCCCAGTTGTTTTCCAATTTCACCGGCTCCGTGGATG ACCGTGGGACCTGCCAGTGCTCTGTTTCCCTGCCAGACACCACCTTTCCCGTGGACAGAGTG GAGGGAATATGTCCAATTAATTAGTGTGTATGAAAAGAAACTGTTAAACCTAACTGTCCGAA TTGACATCATGGAGAAGGATACCATTTCTTACACTGAACTGGACTTCGAGCTGATCAAGGTA GAAGTGAAGGAGATGGAAAAACTGGTCATACAGCTGAAGGAGAGTTTTGGTGGAAGCTCAGA AATTGTTGACCAGCTGGAGGTGGAGATAAGAAATATGACTCTCTTGGTAGAGAAGCTTGAGA CACTAGACAAAAACAATGTCCTTGCCATTCGCCGAGAAATCGTGGCTCTGAAGACCAAGCTG AAAGAGTGTGAGGCCTCTAAAGATCAAAACACCCCTGTCGTCCACCCTCCTCCCACTCCAGG GAGCTGTGGTCATGGTGGTGTGGTGAACATCAGCAAACCGTCTGTGGTTCAGCTCAACTGGA GGACTGTATTGGGTGGCGCCATTGAATACAGATGGGAGACTGTTGGAGTATTATAGACTGTA CAACACACTGGATGATTTGCTATTGTATAAATGCTCGAGAGTTGCGGATCACCTATGGCC **AAGGTAGTGGTACAGCAGTTTAGAACAACAACATGTACGTCAACATGTACAACACCGGGAA**T ATTGCCAGAGTTAACCTGACCACCAACACGATTGCTGTGACTCAAACTCTCCCTAATGCTGC CTATAATAACCGCTTTTCATATGCTAATGTTGCTTGGCAAGATATTGACTTTGCTGTGGATG AGAATGGATTGTGGGTTATTTATTCAACTGAAGCCAGCACTGGTAACATGGTGATTAGTAAA CTCAATGACACCACACTTCAGGTGCTAAACACTTGGTATACCAAGCAGTATAAACCATCTGC TTCTAACGCCTTCATGGTATGTGGGGTTCTGTATGCCACCCGTACTATGAACACCAGAACAG AAGAGATTTTTTACTATTATGACACAAACACAGGGAAAGAGGGGCAAACTAGACATTGTAATG CATAAGATGCAGGAAAAAGTGCAGAGCATTAACTATAACCCTTTTGACCAGAAACTTTATGT CTATAACGATGGTTACCTTCTGAATTATGATCTTTCTGTCTTGCAGAAGCCCCAG<u>TAA</u>GCTG ATATCTGCAGGGGTGTCTAAAAGTGTGTTCATTTTGCAGCAATGTTTAGGTGCATAGTTCTA CCACACTAGAGATCTAGGACATTTGTCTTGATTTGGTGAGTTCTCTTGGGAATCATCTGCCT CTTCAGGCGCATTTTGCAATAAAGTCTGTCTAGGGTGGGATTGTCAGAGGTCTAGGGGCACT GTGGGCCTAGTGAAGCCTACTGTGAGGAGGCTTCACTAGAAGCCTTAAATTAGGAATTAAGG **AACTTAAAACTCAGTATGGCGTCTAGGGATTCTTTGTACAGGAAATATTGCCCAATGACTAG** CACCTGGAATGATGCTTTGTATGTGGCAGATAAGTAAATTTGGCATGCTTATATATTCTACA TCTGTAAAGTGCTGAGTTTTATGGAGAGAGGCCTTTTTATGCATTAAATTGTACATGGCAAA TAAATCCCAGAAGGATCTGTAGATGAGGCACCTGCTTTTTCTTTTCTCTCATTGTCCACCTT AACCAGACTTACTAACCAATTCCACCCCCCACCAACCCCCTTCTACTGCCTACTTTAAAAAA TGGACTTTTATTTACATGACTCTAAGACTATAAGAAAATCTGATGGCAGTGACAAAGTGCTA GCATTTATTGTTATCTAATAAAGACCTTGGAGCATATGTGCAACTTATGAGTGTATCAGTTG TTGCATGTAATTTTTGCCTTTGTTTAAGCCTGGAACTTGTAAGAAAATGAAAATTTAATTTT TTTTTCTAGGACGAGCTATAGAAAAGCTATTGAGAGTATCTAGTTAATCAGTGCAGTAGTTG GAAACCTTGCTGGTGTATGTGATGTGCTTCTGTGCTTTTGAATGACTTTATCATCTAGTCTT TGTCTATTTTTCCTTTGATGTTCAAGTCCTAGTCTATAGGATTGGCAGTTTAAATGCTTTAC

39 /310 **FIGURE 38**

MRPGLSFLLALLFFLGQAAGDLGDVGPPIPSPGFSSFPGVDSSSSFSSSSRSGSSSSRSLGS
GGSVSQLFSNFTGSVDDRGTCQCSVSLPDTTFPVDRVERLEFTAHVLSQKFEKELSKVREYV
QLISVYEKKLLNLTVRIDIMEKDTISYTELDFELIKVEVKEMEKLVIQLKESFGGSSEIVDQ
LEVEIRNMTLLVEKLETLDKNNVLAIRREIVALKTKLKECEASKDQNTPVVHPPPTPGSCGH
GGVVNISKPSVVQLNWRGFSYLYGAWGRDYSPQHPNKGLYWVAPLNTDGRLLEYYRLYNTLD
DLLLYINARELRITYGQGSGTAVYNNNMYVNMYNTGNIARVNLTTNTIAVTQTLPNAAYNNR
FSYANVAWQDIDFAVDENGLWVIYSTEASTGNMVISKLNDTTLQVLNTWYTKQYKPSASNAF
MVCGVLYATRTMNTRTEEIFYYYDTNTGKEGKLDIVMHKMQEKVQSINYNPFDQKLYVYNDG
YLLNYDLSVLQKPQ

40/310 FIGURE 39

FIGURE 40

CCGCTGCTCTTGTGACGTTGTGGAGATGGGGAGCGTCCTGGGGGCTGTGCTCCATGGCGAGCT GGATACCATGTTTGTGTGGAAGTGCCCCGTGTTTGCTATGCCGATGCTGTCCTAGTGGAAAC TGTAATGTTGATACCAGGAATGGAAGAACAACTGAATAAGATTCCTGGATTTTGTGAGAATG AGAAAGGTGTTGTCCCTTGTAACATTTTGGTTGGCTATAAAGCTGTATATCGTTTGTGCTTT GGTTTGGCTATGTTCTATCTTCTCTCTTTTACTAATGATCAAAGTGAAGAGTAGCAGTGA TCCTAGAGCTGCAGTGCACAATGGATTTTGGTTCTTTAAATTTGCTGCAGCAATTGCAATTA TTATTGGGGCATTCTTCATTCCAGAAGGAACTTTTACAACTGTGTGGTTTTATGTAGGCATG GAATGAATCGTGGGTTGAAAAAATGGAAGAAGGGAACTCGAGATGTTGGTATGCAGCCTTGT TATCAGCTACAGCTCTGAATTATCTGCTGTCTTTAGTTGCTATCGTCCTGTTCTTTGTCTAC TACACTCATCCAGCCAGTTGTTCAGAAAACAAGGCGTTCATCAGTGTCAACATGCTCCTCTG CGTTGGTGCTTCTGTAATGTCTATACTGCCAAAAATCCAAGAATCACAACCAAGATCTGGTT TGTTACAGTCTTCAGTAATTACAGTCTACACAATGTATTTGACATGGTCAGCTATGACCAAT GAACCAGAAACAAATTGCAACCCAAGTCTACTAAGCATAATTGGCTACAATACAACAAGCAC TGTCCCAAAGGAAGGCAGTCAGTCCAGTGGTGGCATGCTCAAGGAATTATAGGACTAATTC TCTTTTTGTTGTGTGTATTTTATTCCAGCATCCGTACTTCAAACAATAGTCAGGTTAATAAA CTGACTCTAACAAGTGATGAATCTACATTAATAGAAGATGGTGGAGCTAGAAGTGATGGATC ACTGGAGGATGGGGACGATGTTCACCGAGCTGTAGATAATGAAAGGGATGGTGTCACTTACA GTTATTCCTTCTTCACTTCATGCTTTTCCTGGCTTCACTTTATATCATGATGACCCTTACC AACTGGTCCAGGTATGAACCCTCTCGTGAGATGAAAAGTCAGTGGACAGCTGTCTGGGTGAA AATCTCTTCCAGTTGGATTGGCATCGTGCTGTATGTTTGGACACTCGTGGCACCACTTGTTC TTACAAATCGTGATTTTGAC<u>TGAG</u>TGAGACTTCTAGCATGAAAGTCCCACTTTGATTATTGC TTATTTGAAAACAGTATTCCCAACTTTTGTAAAGTTGTGTATGTTTTTGCTTCCCATGTAAC TTCTCCAGTGTTCTGGCATGAATTAGATTTTACTGCTTGTCATTTTGTTATTTTCTTACCAA GTGCATTGATATGTGAAGTAGAATGAATTGCAGAGGAAAGTTTTATGAATATGGTGATGAGT TAGTAAAAGTGGCCATTATTGGGCTTATTCTCTGCTCTATAGTTGTGAAAATGAAGAGTAAAA GCAAATGTATGGCTGCCTTTTGAAATATTTGATGTGTTGCCTGGCAGGATACTGCAAAGAAC ATGGTTTATTTAAAATTTATAAACAAGTCACTTAAATGCCAGTTGTCTGAAAAATCTTATA AGGTTTTACCCTTGATACGGAATTTACACAGGTAGGGAGTGTTTAGTGGACAATAGTGTAGGTTA TGGATGGAGGTGTCGGTACTAAATTGAATAACGAGTAAATAATCTTACTTGGGTAGAGATGG CCTTTGCCAACAAGTGAACTGTTTTGGTTGTTTTAAACTCATGAAGTATGGGTTCAGTGGA **AATGTTTGGAACTCTGAAGGATTTAGACAAGGTTTTGAAAAGGATAATCATGGGTTAGAAGG** AAGTGTTTTGAAAGTCACTTTGAAAGTTAGTTTTTGGGCCCAGCACGGTAGCTCACCCTTCGT AATCCCAGCACTTTGGGAGCTTAAGTGGGTAGATTACTTGAGCCCAGGAATTCAGACCAGCT TGGCACATGGTGAACCTGTTCTATAAAAATAATCTGGCTTTGAGCATATGCCTGTGGTCCAG CACTGAGAGGCTAGTGAAGATTGCTGAGCCCAGAGCCAAAGGTTGCAGTGAGCAAGTCACGT CAAAATTTTGACAGGGAAGGAAGTAACTGCAAAACCACTAGGCTTTAGTAGGTACTTATATA AAATCTAGTCCAGTTCTCTCATTTAAAAAAAATGAAGACACTGAAATACAGACTTAAATAGCT CAGATAGCTAATTAGGAAATTTCAAGTTGGCCAATAATAGCATTCTCTCTGACATTTAAAAA GTGGATTGCTGGTGTCCAGCATGACCCATAAACAGGTCAGAAGAATGATGGAATGTTTTAGA ATAAACTCCTGCTTATAGTATACTACACAGTTCAAAAGATGTTTAAAATGCTTTTGTATTTA CTGCCATGTAATTGAAATATATAGATTATTGTAACCTTTCAACCTGAAAATCAAGCAGTATG AGAGTTTAGTTATTTGTATGTGTCACTAGTGTCTAATGAAGCTTTTAAAATCTACAATTTCT TCTTTAAAAATATTTATTAATGTGAATGGAATATAACAATTCAGCTTAATTCCCCCAACCTTA AATTCAGAGAAAAAAAAAAAAA

42/3-10

FIGURE 41

MGSVLGLCSMASWIPCLCGSAPCLLCRCCPSGNNSTVTRLIYALFLLVGVCVACVMLIPGME
EQLNKIPGFCENEKGVVPCNILVGYKAVYRLCFGLAMFYLLLSLLMIKVKSSSDPRAAVHNG
FWFFKFAAAIAIIIGAFFIPEGTFTTVWFYVGMAGAFCFILIQLVLLIDFAHSWNESWVEKM
EEGNSRCWYAALLSATALNYLLSLVAIVLFFVYYTHPASCSENKAFISVNMLLCVGASVMSI
LPKIQESQPRSGLLQSSVITVYTMYLTWSAMTNEPETNCNPSLLSIIGYNTTSTVPKEGQSV
QWWHAQGIIGLILFLLCVFYSSIRTSNNSQVNKLTLTSDESTLIEDGGARSDGSLEDGDDVH
RAVDNERDGVTYSYSFFHFMLFLASLYIMMTLTNWSRYEPSREMKSQWTAVWVKISSSWIGI
VLYVWTLVAPLVLTNRDFD

FIGURE 42

GCGAGAAAGAAGCTGTCTCCATCTTGTCTGTATCCCGCTGCTTCTTGNGACGTTGTGGAGAT
GGGGAGCGTCCCTGGGGCTGTGCTCCATGGCGAGCTGGATACCATGTTTGTGTGGAAGTGCC
CCGTGTTTGCTATGCCGATGCTGTCCTAGTGGAAACAANTCCACTGTAACTAGATTGATCTA
TGCACTTTTCTTGCTTGTTGGAGTATGTGTAGCTTGTTAATGTTGATACCAGGAATGGAAG
AACAACTGAATAAGATTCCTGGATTTTGTGAGAATGAGAAAGGTGTTGTCCCTTGTAACATT
TTGGTTGGCTATAAAGCTGTATATCGTTTGTGTTTTGGTTTGGCTATGTTCTTCTT
CTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCACAATGGAT
TTTGGTTCTTTAAATTTGCTGCAGCAATTGCAATTATTTTTTGGGGC

44/3-10 FIGURE 43

GTTATTGTGAACTTTGTGGAGATGGGAGGTCNTGGGGCTGTGTTCCATGGCGAGCTGGATAC
CANGTTTGTGTGGAAGTGCCCCGTGTTTGNTATGCCGATGCTGTCCTAGTGGAAACAANTCC
ACTGTAATTAGATTGATNTATGCACTTTTNTTGCTTGTTGGAGTANGTGTAGCTTGTTAAT
GTTGATACCAGGAATGGAAGAACAACTGAATAAGATTCCTGGATTTTGTGAGAATGAGAAAG
GTGTTGTCCCTTGTAACATTTTGGTTGGCTATAAAGCTGTATATNGTTTGTGCTTTGGTTTG
GCTANGTTCTATNTTCTTCTCTCTTTTACTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAG
AGCTGCAGTGCACAATGGATTTTGGTTTTTAAATTTGCTGCAGCAATTGCAATTATTATTG

FIGURE 44

FIGURE 45

FIGURE 46A

GGCCTCTCCAATGGCAAATGTGTGTGGCTGGAGGCGAGGCGCGAGGCTTTCGGCAAAGGCAGT CGAGTGTTTGCAGACCGGGCGAGTCCTGTGAAAGCAGATAAAAGAAAACATTTATTAACGT GTCATTACGAGGGGAGCGCCCGGCCGGGGCTGTCGCACTCCCCGCGGAACATTTGGCTCCCT CCAGCTCCGAGAGAGAGAAGAAGCGGAAAAGAGGCAGATTCACGTCGTTTCCAGCCA AGTGGACCTGATCGATGGCCCTCCTGAATTTATCACGATATTTGATTTATTAGCGATGCCCC CTGGTTTGTGTGTTACGCACACACGCGCGCACACACGCTCTGGCTCGCTTCCCTCGT TTCCAGCTCCTGGGCGAATCCCACATCTGTTTCAACTCTCCGCCGAGGGCGAGCAGGAGCGA GAGTGTGTCGAATCTGCGAGTGAAGAGGGACGAGGGAAAAGAAACAAAGCCACAGACGCAAC TTGAGACTCCCGCATCCCAAAAGAAGCACCAGATCAGCAAAAAAAGAAGATGGGCCCCCCGA GCCTCGTGCTGCTTGCTGTCCGCAACTGTGTTCTCCCTGCTGGGTGGAAGCTCGGCCTTC CTGTCGCACCACCGCCTGAAAGGCAGGTTTCAGAGGGACCGCAGGAACATCCGCCCCAACAT CATCCTGGTGCTGACGGACGACCAGGATGTGGAGCTGGGTTCCATGCAGGTGATGAACAAGA CCCGCCCATCATGGAGCAGGCCGGGCGCACTTCATCAACGCCTTCGTGACCACACCCATG TGCTGCCCTCACGCTCCTCCATCCTCACTGGCAAGTACGTCCACAACCACAACACCTACAC CAACAATGAGAACTGCTCCTCGCCCTCCTGGCAGGCACACGAGAGCCGCACCTTTGCCG TGTACCTCAATAGCACTGGCTACCGGACAGCTTTCTTCGGGAAGTATCTTAATGAATACAAC GGCTCCTACGTGCCACCCGGCTGGAAGGAGTGGGTCGGACTCCTTAAAAACTCCCGCTTTTA TAACTACACGCTGTCGGAACGGGTGAAAGAGAAGCACGCCTCCGACTACTCCAAGGATT ACCTCACAGACCTCATCACCAATGACAGCGTGAGCTTCTTCCGCACGTCCAAGAAGATGTAC CCGCACAGGCCAGTCCTCATGGTCATCAGCCATGCAGCCCCCCACGGCCCTGAGGATTCAGC CCCACAATATTCACGCCTCTTCCCAAACGCATCTCAGCACATCACGCCGAGCTACAACTACG CGCCCAACCCGGACAAACACTGGATCATGCGCTACACGGGGCCCATGAAGCCCATCCACATG GAATTCACCAACATGCTCCAGCGGAAGCGCTTGCAGACCCTCATGTCGGTGGACGACTCCAT GGAGACGATTTACAACATGCTGGTTGAGACGGCCGAGCTGGACAACACGTACATCGTATACA CCGCCGACCACGGTTACCACATCGGCCAGTTTGGCCTGGTGAAAGGGAAATCCATGCCATAT GAGTTTGACATCAGGGTCCCGTTCTACGTGAGGGGCCCCAACGTGGAAGCCGGCTGTCTGAA TCCCCACATCGTCCTCAACATTGACCTGGCCCCCACCATCCTGGACATTGCAGGCCTGGACA TACCTGCGGATATGGACGGGAAATCCATCCTCAAGCTGCTGGACACGGAGCGGCCGGTGAAT CGGTTTCACTTGAAAAAGAAGATGAGGGTCTGGCGGGACTCCTTCTTGGTGGAGAGAGGCAA GCTGCTACACAAGAGAGACAATGACAAGGTGGACGCCCAGGAGGAGAACTTTCTGCCCAAGT ACCAGCGTGTGAAGGACCTGTGTCAGCGTGCTGAGTACCAGACGGCGTGTGAGCAGCTGGGA CAGAAGTGCAGTGTGTGGAGGACGCCACGGGGAAGCTGAAGCTGCATAAGTGCAAGGGCCC CATGCGGCTGGGCGGCAGCAGAGCCCTCTCCAACCTCGTGCCCAAGTACTACGGGCAGGGCA GCGAGGCCTGCACCTGTGACAGCGGGGACTACAAGCTCAGCCTGGCCGGACGCCGGAAAAAA CTCTTCAAGAAGAAGTACAAGGCCAGCTATGTCCGCAGTCGCTCCATCCGCTCAGTGGCCAT CGAGGTGGACGGCAGGGTGTACCACGTAGGCCTGGTGATGCCCCCCAGCCCCGAAACCTCA CCAAGCGGCACTGGCCAGGGGCCCCTGAGGACCAAGATGACAAGGATGGTGGGGACTTCAGT GGCACTGGAGGCCTTCCCGACTACTCAGCCGCCAACCCCATTAAAGTGACACATCGGTGCTA CATCCTAGAGAACGACAGTCCAGTGTGACCTGGACCTGTACAAGTCCCTGCAGGCCTGGA AAGACCACAAGCTGCACATCGACCACGAGATTGAAACCCTGCAGAACAAAATTAAGAACCTG AGGGAAGTCCGAGGTCACCTGAAGAAAAAGCGGCCAGAAGAATGTGACTGTCACAAAATCAG CTACCACACCCAGCACAAAGGCCGCCTCAAGCACAGAGGCTCCAGTCTGCATCCTTTCAGGA AGGGCCTGCAAGAGAAGGACAAGGTGTGGCTGTTGCGGGAGCAGAAGCGCAAGAAGAAACTC CGCAAGCTGCTCAAGCGCCTGCAGAACAACGACACGTGCAGCATGCCAGGCCTCACGTGCTT CACCCACGACAACCAGCACTGGCAGACGGCGCCTTTCTGGACACTGGGGCCTTTCTGTGCCT GCACCAGCGCCAACAATAACACGTACTGGTGCATGAGGACCATCAATGAGACTCACAATTTC

FIGURE 46B

CTCTTCTGTGAATTTGCAACTGGCTTCCTAGAGTACTTTGATCTCAACACAGACCCCTACCA GCTGATGAATGCAGTGAACACACTGGACAGGGATGTCCTCAACCAGCTACACGTACAGCTCA TGGAGCTGAGGAGCTGCAAGGGTTACAAGCAGTGTAACCCCCGGACTCGAAACATGGACCTG GATGGAGGAAGCTATGAGCAATACAGGCAGTTTCAGCGTCGAAAGTGGCCAGAAATGAAGAG ACCTTCTTCCAAATCACTGGGACAACTGTGGGAAGGCTGGGAAGGT<u>TAA</u>GAAACAACAGAGG TGGACCTCCAAAAACATAGAGGCATCACCTGACTGCACAGGCAATGAAAAACCATGTGGGTG AACATGACAGATTCTGGAGGATAACCAGCAGGAGCAGAGATAACTTCAGGAAGTCCATTTTT GCCCCTGCTTTTGCTTTGGATTATACCTCACCAGCTGCACAAAATGCATTTTTTCGTATCAA GATTTCCTTGGAAATTTCTCCCAAGGGCGAAAGTCATTGGAATTTTTAAATCATAGGGGAAA AGCAGTCCTGTTCTAAATCCTCTTATTCTTTTGGTTTGTCACAAAGAAGAAGAACTAAGAAGCA GGACAGAGGCAACGTGGAGAGGCTGAAAACAGTGCAGAGACGTTTGACAATGAGTCAGTAGC ACAAAAGAGATGACATTTACCTAGCACTATAAACCCTGGTTGCCTCTGAAGAAACTGCCTTC ATTGTATATATGTGACTATTTACATGTAATCAACATGGGAACTTTTAGGGGAACCTAATAAG AAATCCCAATTTTCAGGAGTGGTGGTGTCAATAAACGCTCTGTGGCCAGTGTAAAAGAAAAA

FIGURE 47

MGPPSLVLCLLSATVFSLLGGSSAFLSHHRLKGRFQRDRRNIRPNIILVLTDDQDVELGSMQ
VMNKTRRIMEQGGAHFINAFVTTPMCCPSRSSILTGKYVHNHNTYTNNENCSSPSWQAQHES
RTFAVYLNSTGYRTAFFGKYLNEYNGSYVPPGWKEWVGLLKNSRFYNYTLCRNGVKEKHGSD
YSKDYLTDLITNDSVSFFRTSKKMYPHRPVLMVISHAAPHGPEDSAPQYSRLFPNASQHITP
SYNYAPNPDKHWIMRYTGPMKPIHMEFTNMLQRKRLQTLMSVDDSMETIYNMLVETGELDNT
YIVYTADHGYHIGQFGLVKGKSMPYEFDIRVPFYVRGPNVEAGCLNPHIVLNIDLAPTILDI
AGLDIPADMDGKSILKLLDTERPVNRFHLKKKMRVWRDSFLVERGKLLHKRDNDKVDAQEEN
FLPKYQRVKDLCQRAEYQTACEQLGQKWQCVEDATGKLKLHKCKGPMRLGGSRALSNLVPKY
YGQGSEACTCDSGDYKLSLAGRRKKLFKKKYKASYVRSRSIRSVAIEVDGRVYHVGLGDAAQ
PRNLTKRHWPGAPEDQDDKDGGDFSGTGGLPDYSAANPIKVTHRCYILENDTVQCDLDLYKS
LQAWKDHKLHIDHEIETLQNKIKNLREVRGHLKKKRPEECDCHKISYHTQHKGRLKHRGSSL
HPFRKGLQEKDKVWLLREQKRKKKLRKLLKRLQNNDTCSMPGLTCFTHDNQHWQTAPFWTLG
PFCACTSANNNTYWCMRTINETHNFLFCEFATGFLEYFDLNTDPYQLMNAVNTLDRDVLNQL
HVQLMELRSCKGYKQCNPRTRNMDLDGGSYEQYRQFQRRKWPEMKRPSSKSLGQLWEGWEG

50/310 FIGURE 48

AACAAAGTTCAGTGACTGAGGGGCTGAGCGGAGGCTGCTGAAGGGGAGAAAGGAGTGAGGA ${\tt GCTGCTGGGCAGAGAGGGACTGTCCGGCTCCCAG} \underline{{\tt ATG}} {\tt CTGGGGCAGAGCACAGCCC}$ TCGTGGGATGGATCACAGGTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCCACC TGCCTTTTCCACGGACGGCAGGACTGTGACGTGGAGAGGAACCGTACAGCTGCAGGGGGAAA CCGAGTCCGCCGGGCCCAGCCTTGGCCCTTCCGGCGGGGGCCCACCTGGGAATCTTTCACC ATCACCGTCATCCTGGCCACGTATCTCATGTGCCGAATGTGGGCCTCCACCACCACCACCAC $\texttt{CGCTCGC} \underline{\textbf{TGA}} \texttt{GGCTGCTGTCGCCGGTGCCTGTGGACAGCAGCTGCCCTGCCCTTCCCATCTG}$ TTCCCAGGACAAGTGGACCCCATGTTTCCATGTGGAAGGATGCATCTCTGGGGTGAACGAGG GGAACAATAGACTGGGGCTTGCTCCAGCTGCATTTGCATGGCATGCCCCAGTGTACTATGGC AGCAGAGAATGGAGGAACACTGGGTCTGCAGTGCTGAAGGGTTTGGGGAGTGGAGAGCAAGG GTGCTCTTTCGGGGCTGGACAGCCCGTCTTGTGACAGTGACTCCCAGTGAGCCCCAGAAATG ACAAGCGTGTCTTGGCAGAGCCAGCACAAGTGGATGTGAAGTGCCCGTCTTGACCTCCTC ATCAGGCTGCTGCAGGCCTCTGGCGGGCAGGGCACTGGGAGAGGCCCTGAGAATGTCCTTTT GGTTTGGAGAAGGCAGTGTGAGGCTGCACAGTCAATTCATCGGTGCCTTAGTCCAAGAAAAT

FIGURE 49

 ${\tt MLGLLGSTALVGWITGAAVAVLLLLLLLATCLFHGRQDCDVERNRTAAGGNRVRRAQPWPFR} \\ {\tt RRGHLGIFHHHRHPGHVSHVPNVGLHHHHHPRHTPHHLHHHHHPRHTPHHRHHPRHAR} \\$

52/310 FIGURE 50

 ${\tt GGCGGCTGCTGAGCTGCCTTGAGGTGCAGTGTTGGGGATCCAGAGCC} {\tt ATG}{\tt TCGGACCTGCTA}$ CTACTGGGCCTGATTGGGGGCCTGACTCTCTTACTGCTGCTGACGCTGCTGGCCTTTGCCGG GTACTCAGGGCTACTGGCTGGGGTGGAAGTGAGTGCTGGGTCACCCCCCATCCGCAACGTCA CTGTGGCCTACAAGTTCCACATGGGGGCTCTATGGTGAGACTGGGCGGCTTTTCACTGAGAGC TGCAGCATCTCTCCCAAGCTCCGCTCCATCGCTGTCTACTATGACAACCCCCACATGGTGCC CCCTGATAAGTGCCGATGTGCCGTGGGCAGCATCCTGAGTGAAGGTGAGGAATCGCCCTCCC CTGAGCTCATCGACCTCTACCAGAAATTTGGCTTCAAGGTGTTCTCCTTCCCGGCACCCAGC TGTCCATCCTGCCTTGGACACCTACATCAAGGAGCGGAAGCTGTGTGCCTATCCTCGGCTGG AGATCTACCAGGAAGACCAGATCCATTTCATGTGCCCACTGGCACGGCAGGGAGACTTCTAT GTGCCTGAGATGAAGGAGACAGAGTGGAAATGGCGGGGGCTTGTGGAGGCCATTGACACCCA GGTGGATGGCACAGGAGCTGACACAATGAGTGACACGAGTTCTGTAAGCTTGGAAGTGAGCC CTGGCAGCCGGGAGACTTCAGCTGCCACACTGTCACCTGGGGCGAGCAGCCGTGGCTGGGAT GACGGTGACACCCGCAGCGAGCACAGCTACAGCGAGTCAGGTGCCAGCGGCTCCTCTTTTGA GGAGCTGGACTTGGAGGGCGAGGGGCCCTTAGGGGAGTCACGGCTGGACCCTGGGACTGAGC CCCTGGGGACTACCAAGTGGCTCTGGGAGCCCACTGCCCCTGAGAAGGGCAAGGAG<u>TAA</u>CCC ATGGCCTGCACCCTCCTGCAGTGCAGTTGCTGAGGAACTGAGCAGACTCTCCAGCAGACTCT CCAGCCCTCTTCCTCCTCCTGGGGGGGGGGGGGGTTCCTGAGGGACCTGACTTCCCCTGC TCCAGGCCTCTTGCTAAGCCTTCTCCTCACTGCCCTTTAGGCTCCCAGGGCCAGAGGAGCCA GGGACTATTTTCTGCACCAGCCCCCAGGGCTGCCGCCCCTGTTGTGTCTTTTTTTCAGACTC ACAGTGGAGCTTCCAGGACCCAGAATAAAGCCAATGATTTACTTGTTTCACCTGGAAAAAAA AAAAAAAA

FIGURE 51

MSDLLLLGLIGGLTLLLLTLLAFAGYSGLLAGVEVSAGSPPIRNVTVAYKFHMGLYGETGR LFTESCSISPKLRSIAVYYDNPHMVPPDKCRCAVGSILSEGEESPSPELIDLYQKFGFKVFS FPAPSHVVTATFPYTTILSIWLATRRVHPALDTYIKERKLCAYPRLEIYQEDQIHFMCPLAR QGDFYVPEMKETEWKWRGLVEAIDTQVDGTGADTMSDTSSVSLEVSPGSRETSAATLSPGAS SRGWDDGDTRSEHSYSESGASGSSFEELDLEGEGPLGESRLDPGTEPLGTTKWLWEPTAPEKGKE

54/310 FIGURE 52

FIGURE 53

MTLRPSLLPLHLLLLLLSAAVCRAEAGLETESPVRTLQVETLVEPPEPCAEPAAFGDTLHI HYTGSLVDGRIIDTSLTRDPLVIELGQKQVIPGLEQSLLDMCVGEKRRAIIPSHLAYGKRGF PPSVPADAVVQYDVELIALIRANYWLKLVKGILPLVGMAMVPALLGLIGYHLYRKANRPKVS KKKLKEEKRNKSKKK

56/300 FIGURE 54

CCGAAAGTCCCGTCCGGACCCTCCAAGTGGAGACCCTGGTGGAGCCCCCAGAACCATGTGCC
GAGCCCGCTGCTTTTGGAGACACGCTTCACATACACTACACGGGAAGCTTGGTAGATGGACG
TATTATTGACACCTCCCTGACCAGAGACCCTCTGGTTATAGAACTTGGCCAAAAGCAGGTGA
TTCCAGGTCTGGAGCAGAGTCTTCTCGACATGTGTGTGGGAGAAAGCGAAGGCAATCATT
CCTTCTCACTTGGCCTATGGAAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGT
GCAGTATGACGTGGAGCTGATTGCACTAATCCGAGCCAACTACTGGCTAAAGCTGGTGAAGG
GCATTTTGCCTCTGGTAGGGATGGCCATGGTGCCAGCCCTCCTGGGCCTCATTGGGTATCAC
CTATACAGAAAAGGACCCAATGATCTCCAAAAAGAAGCTCAAGGAAGAAACGAAA
CAAGAGCAAAAAGAAATAATAAATAAATTTTTAAAAAACTTTAAAA

CTGCTGCATCCGGGTGTCTGGAGGCTGTGGCCGTTTTGTTTTCTTGGCTAAAATCGGGGGAG TGAGGCGGCCGGCGCGCGCGCACACCGGGCTCCGGAACCACTGCACGACGGGCTGGACTG ACCTGAAAAAA<u>ATG</u>TCTGGATTTCTAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGG GAAAAGCGCAATACTATTGCTTCCATTGCTGCTGGTGTACTATTTTTTACAGGCTGGTGAT TATCATAGATGCAGCTGTTATTTATCCCACCATGAAAGATTTCAACCACTCATACCATGCCT GTGGTGTTATAGCAACCATAGCCTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGA GGTGATAGTTACAGTGAAGGTTGTCTGGGTCAAACAGGTGCTCGCATTTGGCTTTTCGTTGG TTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTTATGTTG CTAAAGAAAAAGACATAGTATACCCTGGAATTGCTGTATTTTTCCAGAATGCCTTCATCTTT TTGTAATGCCATTTTCTAAACTTATTTCTGAGTGTAGTCTCAGCTTAAAGTTGTGTAATACT AAAATCACGAGAACACCTAAACAACAACCAAAAATCTATTGTGGTATGCACTTGATTAACTT ATAAAATGTTAGAGGAAACTTTCACATGAATAATTTTTGTCAAATTTTATCATGGTATAATT TGTAAAAATAAAAAGAAATTACAAAAGAAATTATGGATTTGTCAATGTAAGTATTTGTCATA TCTGAGGTCCAAAACCACAATGAAAGTGCTCTGAAGATTTAATGTGTTTATTCAAATGTGGT CTCTTCTGTGTCAAATGTTAAATGAAATATAAACATTTTTTAGTTTTTAAAATATTCCGTGG TCAAAATTCTTCCTCACTATAATTGGTATTTACTTTTACCAAAAATTCTGTGAACATGTAAT GTAACTGGCTTTTGAGGGTCTCCCAAGGGGTGAGTGGACGTGTTGGAAGAGAGAAGCACCAT GGTCCAGCCACCAGGCTCCCTGTGTCCCTTCCATGGGAAGGTCTTCCGCTGTGCCTCTCATT CCAAGGGCAGGAAGATGTGACTCAGCCATGACACGTGGTTCTGGTGGGATGCACAGTCACTC CACATCCACCACTG

MSGFLEGLRCSECIDWGEKRNTIASIAAGVLFFTGWWIIIDAAVIYPTMKDFNHSYHACGVI ATIAFLMINAVSNGQVRGDSYSEGCLGQTGARIWLFVGFMLAFGSLIASMWILFGGYVAKEK DIVYPGIAVFFQNAFIFFGGLVFKFGRTEDLWO

TGGACGGACCTGAAAAAAATGTTTGGATTTNTAGAGGGNTTGAGATGTTCAGAATGCATGAC
TGGGGGAAAAGCGCAAATACTATTGCTTCCATTGCTGCTGGTGTANTATTTTTTACAGGCTG
GTGGATTATCATAGATGCAGNTGTTATTTATCCCACCATGAAAGATTTCAACCANTCATACC
ATGCCTGTGGTGTTATAGCAACCATAGCCTTCNTAATGATTAATGCAGTATCGAATGGACAA
GTCCGAGGTGATAGTTACAGTGAAGGTTGTTTGGGTCAAACAGGTGCTCGCATTTGGCTTTT
CGTTGGTTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTT
ATGTTGCTAAAGAAAAAGACATAGTATACCCTGGAATTGNTGTATTTTTCCAGAATGCCTTC
ATCTTTTTTGGAGGGCTGGTTTTTAAGTTTGGCCGCACTGAAGANTTATGGCAGTG

GGACACCGGGTTCCGGACCAATGCANGACGGGGTGGANTGACCTGAAAAAAAATGTTTGGATT
TTTAGAGGGCTTGAGATGNTCAGAATGCATTGACTGGGGGAAAAGCGCAATANTATTGCTTT
CCATTGCTGCTGGTGTACTATTTTTTACAGGGTGGTGGATTATCATAGATGCAGCTGTTATT
TATCCCACCATGAAAGATTTNAACCACTCATACCATGCCTGTGGTGTTATAGCAACCATAGC
CTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTT
GTTTGGGTCAAACAGGTGNTCGCATTTGGCTTTTCGTTGGTTTCATGTTGGCCTTTGGATTT
CTGATTGNATTCTATGCGGATTCTTCTTGGAGGTTATGTTGCTAAAGAAAAAGACATAGTAT
ACCCTGGAATTNCTNTATTTTTCCAGAATGCC

FIGURE 61

TAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGGGAAAAGCGCAATANTATTGCTTCC
ATTGNTGNTGGTGTANTATTTTTTTTACAGGCTGGTGGATTATNATAGATGCAGCTGTTATTT
ATCCCACCATGAAAGATTTNAACCANTCATACCATGCCTGTGGTGTTATAGCAACCATAGCC
TTCCTAATGATTAATGCAGTATNGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTTG
TTTGGGTCAAACAGGTGNTNGCATTTGGCTTTTNGTTGGTTTCATGTTGGCCTTTGGATCTN
TGATTGCATTTATGTGGATTNTTTTTTGGAGGTTATGTTGCTAAAGNAAAAGACATAGTATAC
CCTGT

FIGURE 62

FIGURE 63

TCTGCAAAGTTTACTTGGGACTATTCTCTGGCAGCTCCCCGAATCCTTTCTCCGAAGATGTC AAACGGCCCCCAGCGCCCCTGGTAACTGACAAGGAGGCCCAGGAAGAAGGTTCTCAAACAAGC TTTTTCAGCCAACCAAGTGCCGGAGAAGCTGGATGTGGTGGTAATTGGCAGTGGCTTTGGGG GCCTGGCTGCAGCTGCAATTCTAGCTAAAGCTGGCAAGCGAGTCCTGGTGCTGGAACAACAT ACCAAGGCAGGGGGCTGCTGTCATACCTTTGGAAAGAATGGCCTTGAATTTGACACAGGAAT CCATTACATTGGGCGTATGGAAGAGGGCAGCATTGGCCGTTTTATCTTGGACCAGATCACTG AAGGGCAGCTGGACTGGGCTCCCCTGTCCTCTCTTTTGACATCATGGTACTGGAAGGGCCC AATGGCCGAAAGGAGTACCCCATGTACAGTGGAGAGAAAGCCTACATTCAGGGCCTCAAGGA GAAGTTTCCACAGGAGGAAGCTATCATTGACAAGTATATAAAGCTGGTTAAGGTGGTATCCA GTGGAGCCCCTCATGCCATCCTGTTGAAATTCCTCCCATTGCCCGTGGTTCAGCTCCTCGAC AGGTGTGGGCTGCTGACTCGTTTCTCTCCATTCCTTCAAGCATCCACCCAGAGCCTGGCTGA GGTCCTGCAGCAGCTGGGGGCCTCCTCTGAGCTCCAGGCAGTACTCAGCTACATCTTCCCCA CTTACGGTGTCACCCCAACCACAGTGCCTTTTCCATGCACGCCCTGCTGGTCAACCACTAC ATGAAAGGAGGCTTTTATCCCCGAGGGGGTTCCAGTGAAATTGCCTTCCACACCATCCCTGT GATTCAGCGGGCTGGGGGCCTGTCCTCACAAAGGCCACTGTGCAGAGTGTGTTGCTGGACT CAGCTGGGAAAGCCTGTGGTGTCAGTGTGAAGAAGGGGGCATGAGCTGGTGAACATCTATTGC CCCATCGTGGTCTCCAACGCAGGACTGTTCAACACCTATGAACACCTACTGCCGGGGAACGC CCGCTGCCTGCCAGGTGTGAAGCAGCAACTGGGGACGGTGCGGCCCGGCTTAGGCATGACCT CTGTTTTCATCTGCCTGCGAGGCACCAAGGAAGACCTGCATCTGCCGTCCACCAACTACTAT GTTTACTATGACACGGACATGGACCAGGCGATGGAGCGCTACGTCTCCATGCCCAGGGAAGA GGCTGCGGAACACATCCCTCTTCTCTTCTTCTCCCATCAGCCAAAGATCCGACCTGGG AGGACCGATTCCCAGGCCGGTCCACCATGATCATGCTCATACCCACTGCCTACGAGTGGTTT GAGGAGTGGCAGGCGGAGCTGAAGGGAAAGCGGGGCAGTGACTATGAGACCTTCAAAAACTC CTTTGTGGAAGCCTCTATGTCAGTGGTCCTGAAACTGTTCCCACAGCTGGAGGGGAAGGTGG AGAGTGTGACTGCAGGATCCCCACTCACCAACCAGTTCTATCTGGCTGCTCCCCGAGGTGCC TGCTACGGGGCTGACCATGACCTGGGCCGCCTGCACCCTTGTGTGATGGCCTCCTTGAGGGC CCAGAGCCCCATCCCCAACCTCTATCTGACAGGCCAGGATATCTTCACCTGTGGACTGGTCG GGGCCCTGCAAGGTGCCCTGCTGTGCAGCAGCGCCATCCTGAAGCGGAACTTGTACTCAGAC CTTAAGAATCTTGATTCTAGGATCCGGGCACAGAAGAAAAAGAAT<u>TAG</u>TTCCATCAGGGAGG AGTCAGAGGAATTTGCCCAATGGCTGGGGCATCTCCCTTGACTTACCCATAATGTCTTTCTG CATTAGTTCCTTGCACGTATAAAGCACTCTAATTTGGTTCTGATGCCTGAAGAGAGGCCTAG TTTAAATCACAATTCCGAATCTGGGGCAATGGAATCACTGCTTCCAGCTGGGGCAGGTGAGA TCTTTACGCCTTTTATAACATGCCATCCCTACTAATAGGATATTGACTTGGATAGCTTGATG TCTCATGACGAGCGGCGCTCTGCATCCCTCACCCATGCCTCCTAACTCAGTGATCAAAGCGA ATATTCCATCTGTGGATAGAACCCCTGGCAGTGTTGTCAGCTCAACCTGGTGGGTTCAGTTC TGTCCTGAGGCTTCTGCTCTCATTCATTTAGTGCTACGCTGCACAGTTCTACACTGTCAAGG GAAAAGGGAGACTAATGAGGCTTAACTCAAAACCTGGGCGTGGTTTTGGTTGCCATTCCATA GGTTTGGAGAGCTCTAGATCTCTTTTGTGCTGGGTTCAGTGGCTCTTCAGGGGACAGGAAAT GCCTGTGTCTGGCCAGTGTGGTTCTGGAGCTTTGGGGTAACAGCAGGATCCATCAGTTAGTA CTTATCCACCAAATACACAGGGAAGGGTGATGCAGGGAAGGGTGACATCAGGAGTCAGGGCA TGGACTGGTAAGATGAATACTTTGCTGGGCTGAAGCAGGCTGCAGGGCATTCCAGCCAAGGG AAGCCACGGAATGTGTGTGAAGCCCAGAAATGGCATTTGCAGTTAATTAGCACATGTGAGGG TTAGACAGGTAGGTGAATGCAAGCTCAAGGTTTGGAAAAATGACTTTTCAGTTATGTCTTTG GTATCAGACATACGAAAGGTCTCTTTGTAGTTCGTGTTAATGTAACATTAATAAATTTATTG ATTCCATTGCTTTAAAAAAAAAAAAAAAAA

FIGURE 64

MWLPLVLLLAVLLLAVLCKVYLGLFSGSSPNPFSEDVKRPPAPLVTDKEARKKVLKQAFSAN QVPEKLDVVVIGSGFGGLAAAAILAKAGKRVLVLEQHTKAGGCCHTFGKNGLEFDTGIHYIG ${\tt RMEEGSIGRFILDQITEGQLDWAPLSSPFDIMVLEGPNGRKEYPMYSGEKAYIQGLKEKFPQ}$ EEAIIDKYIKLVKVVSSGAPHAILLKFLPLPVVQLLDRCGLLTRFSPFLQASTQSLAEVLQQ LGASSELQAVLSYIFPTYGVTPNHSAFSMHALLVNHYMKGGFYPRGGSSEIAFHTIPVIQRA GGAVLTKATVQSVLLDSAGKACGVSVKKGHELVNIYCPIVVSNAGLFNTYEHLLPGNARCLP GVKQQLGTVRPGLGMTSVFICLRGTKEDLHLPSTNYYVYYDTDMDQAMERYVSMPREEAAEH IPLLFFAFPSAKDPTWEDRFPGRSTMIMLIPTAYEWFEEWQAELKGKRGSDYETFKNSFVEA SMSVVLKLFPQLEGKVESVTAGSPLTNQFYLAAPRGACYGADHDLGRLHPCVMASLRAQSPI PNLYLTGQDIFTCGLVGALQGALLCSSAILKRNLYSDLKNLDSRIRAQKKKN

GCAGCGGCGAGGCGGCGGTGGTGGCTGAGTCCGTGGTGGCAGAGGCGAAGGCGACAGCTCTA GGGGTTGGCACCGGCCCCGAGAGGAGGATGCGGGTCCGGATAGGGCTGACGCTGCTGCTGTG TGCGGTGCTGCTGAGCTTGGCCTCGGCGTCCTCGGATGAAGAAGGCAGCCAGGATGAATCCT GTAGTTGCTGGTCAAATATTTCTTGATTCAGAAGAATCTGAATTAGAATCCTCTATTCAAGA AGAGGAAGACAGCCTCAAGAGCCAAGAGGGGGGAAAGTGTCACAGAAGATATCAGCTTTCTAG ACCGCCATTGAAGGCACAGCACATGGGGAGCCCTGCCACTTCCCTTTTCTTTTCCTAGATAA GGAGTATGATGAATGTACATCAGATGGGAGGGAAGATGGCAGACTGTGGTGTGCTACAACCT ATGACTACAAAGCAGATGAAAAGTGGGGCTTTTTGTGAAACTGAAGAAGAGGCTGCTAAGAGA CGGCAGATGCAGGAAGCAGAAATGATGTATCAAACTGGAATGAAAATCCTTAATGGAAGCAA CCAAAGCCCTGGAGAGAGTGTCATATGCTCTTTTATTTGGTGATTACTTGCCACAGAATATC CAGGCAGCAGAGAGATGTTTGAGAAGCTGACTGAGGAAGGCTCTCCCAAGGGACAGACTGC TCTTGGCTTTCTGTATGCCTCTGGACTTGGTGTTAATTCAAGTCAGGCAAAGGCTCTTGTAT ATTATACATTTGGAGCTCTTGGGGGCAATCTAATAGCCCACATGGTTTTGGTAAGTAGACTT TAGTGGAAGGCTAATAATATTAACATCAGAAGAATTTGTGGTTTATAGCGGCCACAACTTTT ATTCTTGTTAATGGATATAACACATGGAATCTACATGTAAATGAAAGTTGGTGGAGTCCACA ATTTTTCTTTAAAATGATTAGTTTGGCTGATTGCCCCTAAAAAGAGAGATCTGATAAATGGC TCTTTTTAAATTTTCTCTGAGTTGGAATTGTCAGAATCATTTTTTACATTAGATTATCATAA TTTTAAAAATTTTTCTTTAGTTTTTCAAAATTTTGTAAATGGTGGCTATAGAAAAACAACAT GAAATATTATACAATATTTTGCAACAATGCCCTAAGAATTGTTAAAATTCATGGAGTTATTT GTGCAGAATGACTCCAGAGAGCTCTACTTTCTGTTTTTTACTTTTCATGATTGGCTGTCTTC CCATTTATTCTGGTCATTTATTGCTAGTGACACTGTGCCTGCTTCCAGTAGTCTCATTTTCC CTATTTTGCTAATTTGTTACTTTTTCTTTGCTAATTTGGAAGATTAACTCATTTTTAATAAA ΑΛΑΛΑΛΑΛΑΛΑΛΑΛΑΛΑΛΑΛΑΛΑΛΑΛΑΛΑ

MRVRIGLTLLLCAVLLSLASASSDEEGSQDESLDSKTTLTSDESVKDHTTAGRVVAGQIFLD SEESELESSIQEEEDSLKSQEGESVTEDISFLESPNPENKDYEEPKKVRKPALTAIEGTAHG EPCHFPFLFLDKEYDECTSDGREDGRLWCATTYDYKADEKWGFCETEEEAAKRRQMQEAEMM YQTGMKILNGSNKKSQKREAYRYLQKAASMNHTKALERVSYALLFGDYLPQNIQAAREMFEK LTEEGSPKGQTALGFLYASGLGVNSSQAKALVYYTFGALGGNLIAHMVLVSRL

FIGURE 67

FIGURE 68

 ${\tt MACRCLSFLLMGTFLSVSQTVLAQLDALLVFPGQVAQLSCTLSPQHVTIRDYGVSWYQQRAGSAPRYLLYYRSEEDHHRPADIPDRFSAAKDEAHNACVLTISPVQPEDDADYYCSVGYGFSP.}$

FIGURE 69

GCCGCCCCGAGACCGGGCCCGGGGGCGCGGGGCGCGGATGCGGCGCCCCGGGGCGCG CGCTGCTGCTGGGGGCCTTCCCACCGGCCGCCGCCCGAGGCCCCCAAAGATGGCGGAC AAGGTGGTCCCACGGCAGGTGGCCCGGCTGGGCCGCACTGTGCGGCTGCAGTGGC GGGGGACCCGCCGCCGCTGACCATGTGGACCAAGGATGGCCGCACCATCCACAGCGGCTGGA GCCGCTTCCGCGTGCTGCCGCAGGGGCTGAAGGTGAAGCAGGTGGAGCGGAGGATGCCGGC GTGTACGTGTGCAAGGCCACCAACGGCTTCGGCAGCCTGAGCGTCAACTACACCCTCGTCGT GCTGGATGACATTAGCCCAGGGAAGGAGGCCTGGGGGCCCGACAGCTCCTCTGGGGGTCAAG AGGACCCCGCCAGCCAGCAGTGGGCACGACCGCGCTTCACACAGCCCTCCAAGATGAGGCGC CGGGTGATCGCACGGCCCGTGGGTAGCTCCGTGCGGCTCAAGTGCGTGGCCAGCGGCACCC TCGGCCCGACATCACGTGGATGAAGGACGACCAGGCCTTGACGCGCCCAGAGGCCGCTGAGC CCAGGAAGAAGAAGTGGACACTGAGCCTGAAGAACCTGCGGCCGGAGGACAGCGGCAAATAC ACCTGCCGCGTGTCGAACCGCGCGGGCGCCATCAACGCCACCTACAAGGTGGATGTGATCCA GCGGACCCGTTCCAAGCCCGTGCTCACAGGCACGCACCCCGTGAACACGACGGTGGACTTCG GGGGGACCACGTCCTTCCAGTGCAAGGTGCGCAGCGACGTGAAGCCGGTGATCCAGTGGCTG AAGCGCGTGGAGTACGGCGCCGAGGGCCGCCACAACTCCACCATCGATGTGGGCGGCCAGAA GTTTGTGGTGCCCACGGGTGACGTGTGGTCGCGGCCCGACGGCTCCTACCTCAATAAGC TGCTCATCACCCGTGCCCGCCAGGACGATGCGGGCATGTACATCTGCCTTGGCGCCAACACC ATGGGCTACAGCTTCCGCAGCGCCTTCCTCACCGTGCTGCCAGACCCCAAAACCGCCAGGGCC ACCTGTGGCCTCGTCCTCGGCCACTAGCCTGCCGTGGCCCGTGGTCATCGGCATCCCAG CCGGCGCTGTCTTCATCCTGGGCACCCTGCTCCTGTGGCTTTGCCAGGCCCAGAAGAAGCCC TGCACCCCGCGCCTGCCCTGCCTGGGCACCGCCGGCGGGGACGGCCCGCGACCG CAGCGGAGACAAGGACCTTCCCTCGTTGGCCGCCCTCAGCGCTGGCCCTGGTGTGGGGCCTGT GTGAGGAGCATGGGTCTCCGGCAGCCCCCAGCACTTACTGGGCCCAGGCCCAGTTGCTGGC ACACTCACACGTGGAGGGCAAGGTCCACCAGCACATCCACTATCAGTGCTAGACGGCACCGT ATCTGCAGTGGGCACGGGGGGCCGGCCAGACAGGCAGACTGGGAGGATGGAGGACGGAGCT GCAGACGAAGGCAGGGACCCATGGCGAGGAGGAATGGCCAGCACCCCAGGCAGTCTGTGTG TGAGGCATAGCCCCTGGACACACACACACACACACACACTACCTGGATGCATGTATGCAC ACACATGCGCGCACACGTGCTCCCTGAAGGCACACGTACGCACACGCACATGCACAGATATG CCGCCTGGGCACACAGATAAGCTGCCCAAATGCACGCACACGCACAGAGACATGCCAGAACA TACAAGGACATGCTGCCTGAACATACACACGCACACCCATGCGCAGATGTGCTGCCTGGACA CACACACACACGGATATGCTGTCTGGACGCACACACGTGCAGATATGGTATCCGGACACA ATATTGCCTGGACACACACACACACGCGTGCACAGATATGCTGTCTGGACACGCACAC ACATGCAGATATGCTGCCTGGACACACACTTCCAGACACACGTGCACAGGCGCAGATATGCT ACACACAGATAATGCTGCCTCAACACTCACACGTGCAGATATTGCCTGGACACACA TGTGCACAGATATGCTGTCTGGACATGCACACGCGTGCAGATATGCTGTCCGGATACACACG GCAGATATGCTGCCTGGACACACACACAGATAATGCTGCCTCAACACTCACACACGTGCAGA TATTGCCTGGACACACACATGTGCACAGATATGCTGTCTGGACATGCACACACGTGCAGATA TGCTGTCCGGATACACACGCACGCACACATGCAGATATGCTGCCTGGGCACACACTTCCGGA CACACATGCACACAGGTGCAGATATGCTGCCTGGACACGCAGACTGACGTGCTTTTGG GAGGGTGTGCCGTGAAGCCTGCAGTACGTGTGCCGTGAGGCTCATAGTTGATGAGGGACTTT CCCTGCTCACCGTCACTCCCCCAACTCTGCCCGCCTCTGTCCCCGCCTCAGTCCCCGCCTC CATCCCCGCCTCTGTCCCCTGGCCTTGGCGGCTATTTTTGCCACCTGCCTTGGGTGCCCAGG AGTCCCCTACTGCTGGGGCTGGGGTTGGGGGCACAGCCCCAAGCCTGAGAGGCTGGAG CCCATGGCTAGTGGCTCATCCCCAGTGCATTCTCCCCCTGACACAGAGAAGGGGCCTTGGTA TTTATATTTAAGAAATGAAGATAATATTAATAATGATGGAAGGAAGACTGGGTTGCAGGGAC TGTGGTCTCTCCTGGGGCCCGGGACCCGCCTGGTCTTTCAGCCATGCTGATGACCACACCCC GTCCAGGCCAGACACCCCCCCCCCCCCCCCCCGCTGTCGTGGCCCCAGATCTCTGTAATTTTA

MTPSPLLLLLPPLLLGAFPPAAAARGPPKMADKVVPRQVARLGRTVRLQCPVEGDPPPLTM
WTKDGRTIHSGWSRFRVLPQGLKVKQVEREDAGVYVCKATNGFGSLSVNYTLVVLDDISPGK
ESLGPDSSSGGQEDPASQQWARPRFTQPSKMRRRVIARPVGSSVRLKCVASGHPRPDITWMK
DDQALTRPEAAEPRKKKWTLSLKNLRPEDSGKYTCRVSNRAGAINATYKVDVIQRTRSKPVL
TGTHPVNTTVDFGGTTSFQCKVRSDVKPVIQWLKRVEYGAEGRHNSTIDVGGQKFVVLPTGD
VWSRPDGSYLNKLLITRARQDDAGMYICLGANTMGYSFRSAFLTVLPDPKPPGPPVASSSSA
TSLPWPVVIGIPAGAVFILGTLLLWLCQAQKKPCTPAPAPPLPGHRPPGTARDRSGDKDLPS
LAALSAGPGVGLCEEHGSPAAPQHLLGPGPVAGPKLYPKLYTDIHTHTHTHSHTHSHVEGKV
HQHIHYQC

FIGURE 71A

CCCAGCTGAGGAGCCCTGCTCAAGACACGGTCACTGGATCTGAGAAACTTCCCAGGGGACCG CATTCCAGAGTCAGTGACTCTGTGAAGCACCCACATCTACCTCTTGCCACGTTCCCACGGGC TCTGTGTTGGGGAGACAGACGATGCTCACCCAGTCAGTAAGAAGAGTCCAGCCTGGGAAGAA GAACCCCAGCATCTTTGCCAAGCCTGCCGACACCCTGGAGAGCCCTGGTGAGTGGACAACAT GGTTCAACATCGACTACCCAGGCGGGAAGGGCGACTATGAGCGGCTGGACGCCATTCGCTTC ACCTGCGGCAGCACTGGCCAGGTGGTCCATGGTAGTCCCCGTGAGGGTTTCTGGTGCCTCA ACAGGGAGCAGCGGCCTGGCCAGAACTGCTCTAATTACACCGTACGCTTCCTCTGCCCACCA GGATCCCTGCGCCGAGACACAGAGCGCATCTGGAGCCCATGGTCTCCCTGGAGCAAGTGCTC AGCTGCCTGTGGTCAGACTGGGGTCCAGACTCGCACACGCATTTGCTTGGCAGAGATGGTGT CGCTGTGCAGTGAGGCCAGCGAAGAGGGTCAGCACTGCATGGGCCCAGGACTGTACAGCCTGT GACCTGACCTGCCCAATGGGCCAGGTGAATGCTGACTGTGATGCCTGCATGTGCCAGGACTT CATGCTTCATGGGGCTGTCTCCCTTCCCGGAGGTGCCCCAGCCTCAGGGGCTGCTATCTACC GGCTTGTGCCCTGATGCCAAAAGCATCCTGAAGATCACAAAGGTCAAGTTTGCCCCCATTGT **ACTCACAATGCCCAAGACTAGCCTGAAGGCAGCCACCATCAAGGCAGAGTTTGTGAGGGCAG** AGACTCCATACATGGTGATGAACCCTGAGACAAAAGCACGGAGAGCTGGGCAGAGCGTGTCT CTGTGCTGTAAGGCCACAGGGAAGCCCAGGCCAGACAAGTATTTTTGGTATCATAATGACAC ATTGCTGGATCCTTCCCTCTACAAGCATGAGAGCAAGCTGGTGCTGAGGAAACTGCAGCAGC ACCAGGCTGGGGAGTACTTTTGCAAGGCCCAGAGTGATGCTGGGGCTGTGAAGTCCAAGGTT GCCCAGCTGATTGTCACAGCATCTGATGAGACTCCTTGCAACCCAGTTCCTGAGAGCTATCT TATCCGGCTGCCCATGATTGCTTTCAGAATGCCACCAACTCCTTCTACTATGACGTGGGAC GCTGCCCTGTTAAGACTTGTGCAGGGCAGCAGGATAATGGGATCAGGTGCCGTGATGCTGTG CAGAACTGCTGTGGCATCTCCAAGACAGAGGGAAAGGGAGATCCAGTGCAGTGGCTACACGCT ACCACCAAGGTGGCCAAGGAGTGCAGCTGCCAGCGGTGTACGGAAACTCGGAGCATCGTGC GGGGCCGTGTCAGTGCTGCTGACAATGGGGAGCCCATGCGCTTTGGCCATGTGTACATGGGG AACAGCCGTGTAAGCATGACTGGCTACAAGGGCACTTTCACCCTCCATGTCCCCCAGGACAC TGAGAGGCTGGTGCTCACATTTGTGGACAGGCTGCAGAAGTTTGTCAACACCACCAAAGTGC TACCTTTCAACAAGAAGGGGAGTGCCGTGTTCCATGAAATCAAGATGCTTCGTCGGAAAGAG CCCCATGGCTGAACTGGAGATTCCATCCAGGAGTTTCTACAGGCAGAATGGGGAGCCCTACA TAGGAAAAGTGAAGGCCAGTGTGACCTTCCTGGATCCCGGGAATATTTCCACAGCCACAGCT GCCCAGACTGACCTGAACTTCATCAATGACGAAGGAGACACTTTCCCCCTTCGGACGTATGG CATGTTCTCTGTGGACTTCAGAGATGAGGTCACCTCAGAGCCACTTAATGCTGGCAAAGTGA **AGGTCCACCTTGACTCGACCCAGGTCAAGATGCCAGAGCACATATCCACAGTGAAACTCTGG** TCACTCAATCCAGACACAGGGCTGTGGGAGGAGGAAGGTGATTTCAAATTTGAAAATCAAAG GAGGAACAAAGAGAAGACAGAACCTTCCTGGTGGGCAACCTGGAGATTCGTGAGAGGAGGC TCTTTAACCTGGATGTTCCTGAAAGCAGGCGGTGCTTTGTTAAGGTGAGGGCCTACCGGAGT GAGAGGTTCTTGCCTAGTGAGCAGATCCAGGGGGTTGTGATCTCCGTGATTAACCTGGAGCC TAGAACTGGCTTCTTGTCCAACCCTAGGGCCTGGGGCCGCTTTGACAGTGTCATCACAGGCC CCAACGGGCCTGTGTGCCTGCCTTCTGTGATGACCAGTCCCCTGATGCCTACTCTGCCTAT GTCTTGGCAAGCCTGGCTGGGGAGGAACTGCAAGCAGTGGAGTCTTCTCCTAAATTCAACCC AGGATCCACGGGTTAAAAAGACAGCTTTCCAGATTAGCATGGCCAAGCCAAGGCCCAACTCA GCTGAGGAGAGCAATGGGCCCATCTATGCCTTTGAGAACCTCCGGGCATGTGAAGAGGCACC ACCCAGTGCAGCCCACTTCCGGTTCTACCAGATTGAGGGGGATCGATATGACTACAACACAG TCCCCTTCAACGAAGATGACCCTATGAGCTGGACTGAAGACTATCTGGCATGGTGGCCAAAG CCGATGGAATTCAGGGCCTGCTATATCAAGGTGAAGATTGTGGGGCCACTGGAAGTGAATGT GCGATCCCGCAACATGGGGGGCACTCATCGGCGGACAGTGGGGAAGCTGTATGGAATCCGAG ATGTGAGGAGCACTCGGGACAGGGACCAGCCCAATGTCTCAGCTGCCTGTCTGGAGTTCAAG TGCAGTGGGATGCTCTATGATCAGGACCGTGTGGACCGCACCCTGGTGAAGGTCATCCCCCA GGGCAGCTGCCGTCGAGCCAGTGTGAACCCCATGCTGCATGAGTACCTGGTCAACCACTTGC CACTTGCAGTCAACAACGACACCAGTGAGTACACCATGCTGGCACCCTTGGACCCACTGGGC CACAACTATGGCATCTACACTGTCACTGACCAGGACCCTCGCACGGCCAAGGAGATCGCGCT CGGCCGGTGCTTTGATGGCACATCCGATGGCTCCTCCAGAATCATGAAGAGCAATGTGGGAG TAGCCCTCACCTTCAACTGTGTAGAGAGGCAAGTAGGCGGCCAGAGTGCCTTCCAGTACCTC CAAAGCACCCAGCCCAGTCCCCTGCTGCAGGCACTGTCCAAGGAAGAGTGCCCTCGAGGAG GCAGCAGCGAGCAGGGGTGGCCAGCGTGGAGTGGTGGCCTCTCTGAGATTTC

FIGURE 71B

MVGTKAWVFSFLVLEVTSVLGROTMLTOSVRRVOPGKKNPSIFAKPADTLESPGEWTTWFNI DYPGGKGDYERLDAIRFYYGDRVCARPLRLEARTTDWTPAGSTGQVVHGSPREGFWCLNREQ RPGONCSNYTVRFLCPPGSLRRDTERIWSPWSPWSKCSAACGOTGVOTRTRICLAEMVSLCS EASEEGOHCMGODCTACDLTCPMGOVNADCDACMCQDFMLHGAVSLPGGAPASGAAIYLLTK TPKLLTOTDSDGRFRIPGLCPDGKSILKITKVKFAPIVLTMPKTSLKAATIKAEFVRAETPY MVMNPETKARRAGOSVSLCCKATGKPRPDKYFWYHNDTLLDPSLYKHESKLVLRKLOOHOAG EYFCKAOSDAGAVKSKVAOLIVTASDETPCNPVPESYLIRLPHDCFQNATNSFYYDVGRCPV KTCAGOODNGIRCRDAVONCCGISKTEEREIOCSGYTLPTKVAKECSCORCTETRSIVRGRV SAADNGEPMRFGHVYMGNSRVSMTGYKGTFTLHVPODTERLVLTFVDRLOKFVNTTKVLPFN KKGSAVFHEIKMLRRKEPITLEAMETNIIPLGEVVGEDPMAELEIPSRSFYRONGEPYIGKV KASVTFLDPRNISTATAAOTDLNFINDEGDTFPLRTYGMFSVDFRDEVTSEPLNAGKVKVHL DSTOVKMPEHISTVKLWSLNPDTGLWEEEGDFKFENORRNKREDRTFLVGNLEIRERRLFNL DVPESRRCFVKVRAYRSERFLPSEQIQGVVISVINLEPRTGFLSNPRAWGRFDSVITGPNGA CVPAFCDDOSPDAYSAYVLASLAGEELQAVESSPKFNPNAIGVPQPYLNKLNYRRTDHEDPR VKKTAFOISMAKPRPNSAEESNGPIYAFENLRACEEAPPSAAHFRFYOIEGDRYDYNTVPFN EDDPMSWTEDYLAWWPKPMEFRACYIKVKIVGPLEVNVRSRNMGGTHRRTVGKLYGIRDVRS TRDRDQPNVSAACLEFKCSGMLYDQDRVDRTLVKVIPQGSCRRASVNPMLHEYLVNHLPLAV NNDTSEYTMLAPLDPLGHNYGIYTVTDQDPRTAKEIALGRCFDGTSDGSSRIMKSNVGVALT FNCVEROVGROSAFOYLOSTPAOSPAAGTVOGRVPSRROORASRGGOROGGVVASLRFPRVA QQPLIN

CTGCAAGTTGTTAACGCCTAACACACAAGTATGTTAGGCTTCCACCAAAGTCCTCAATATAC CTGAATACGCACAATATCTTAACTCTTCATATTTGGTTTTGGGATCTGCTTTGAGGTCCCAT ${\tt TTACAAAGAATTTAGAG\underline{ATG}TATTTGTCAAGATCCCTGTCGATTCATGCCCTTTGGGTTACG}$ GTGTCCTCAGTGATGCAGCCCTACCCTTTGGTTTGGGGACATTATGATTTGTGTAAGACTCA GATTTACACGGAAGAAGGGAAAGTTTGGGATTACATGGCCTGCCAGCCGGAATCCACGGACA TGACAAAATATCTGAAAGTGAAACTCGATCCTCCGGATATTACCTGTGGAGACCCTCCTGAG ACGTTCTGTGCAATGGGCAATCCCTACATGTGCAATAATGAGTGTGATGCGAGTACCCCTGA AGTCTGCCACTTGGAAGGAGTATCCCAAGCCTCTCCAGGTTAACATCACTCTGTCTTGGAGC AAAACCATTGAGCTAACAGACAACATAGTTATTACCTTTGAATCTGGGCGTCCAGACCAAAT GATCCTGGAGAAGTCTCTCGATTATGGACGAACATGGCAGCCCTATCAGTATTATGCCACAG ACTGCTTAGATGCTTTTCACATGGATCCTAAATCCGTGAAGGATTTATCACAGCATACGGTC TTAGAAATCATTTGCACAGAAGAGTACTCAACAGGGTATACAACAAATAGCAAAATAATCCA CTTTGAAATCAAAGACAGGTTCGCGCTTTTTGCTGGACCTCGCCTACGCAATATGGCTTCCC TCTACGGACAGCTGGATACAACCAAGAAACTCAGAGATTTCTTTACAGTCACAGACCTGAGG ATAAGGCTGTTAAGACCAGCCGTTGGGGAAATATTTGTAGATGAGCTACACTTGGCACGCTA CTTTTACGCGATCTCAGACATAAAGGTGCGAGGAAGGTGCAAGTGTAATCTCCATGCCACTG TATGTGTGTATGACAACAGCAAATTGACATGCGAATGTGAGCACAACACTACAGGTCCAGAC TGTGGGAAATGCAAGAAGAATTATCAGGGCCGACCTTGGAGTCCAGGCTCCTATCTCCCCAT CCCCAAAGGCACTGCAAATACCTGTATCCCCAGTATTTCCAGTATTGGTACGAATGTCTGCG ACAACGAGCTCCTGCACTGCCAGAACGGAGGGACGTGCCACAACAACGTGCGCTGCCTGTGC CCGGCCGCATACACGGGCATCCTCTGCGAGAAGCTGCGGTGCGAGGAGGCTGGCAGCTGCGG $\tt CTCCGACTCTGGCCAGGGCGCCCCCGCACGCACCCCAGCGCTGCTGCTGACCACGC$ ${\tt TGCTGGGAACCGCCAGCCCCCTGGTGTTC}$ AGACACCCCCACTCAGACAGTGTACAAACTAAGAAGGCCTAACTGAACTAAGCCATATTTAT CACCCGTGGACAGCACATCCGAGTCAAGACTGTTAATTTCTGACTCCAGAGGAGTTGGCAGC TGTTGATATTATCACTGCAAATCACATTGCCAGCTGCAGAGCATATTGTGGATTGGAAAGGC TGCGACAGCCCCCAAACAGGAAAGACAAAAAAACAAATCAACCGACCTAAAAAACATTG ${\tt TTCTTTGCTGTCAGGTGCATTGTGGGCATAAGGAAATCTGTTACAAGCTGCCATATTGGCCT}$ GCTTCCGTCCCTGAATCCCTTCCAACCTGTGCTTTAGTGAACGTTGCTCTGTAACCCTCGTT GGTTGAAAGATTTCTTTGTCTGATGTTAGTGATGCACATGTGTAACAGCCCCCTCTAAAAGC GCAAGCCAGTCATACCCCTGTATATCTTAGCAGCACTGAGTCCAGTGCGAGCACACCCCAC ATTTTTCTTGAACTACTGTAATATGTAGATTTTTTTGTATTATTGCCAATTTGTGTTACCAGA CAATCTGTTAATGTATCTAATTCGAATCAGCAAAGACTGACATTTTATTTTGTCCTCTTTCG GAATATCAGTTTACATATAACAAGTGTAATAAGATTCCACCAAAGGACATTCTAAATGTT TTCTTGTTGCTTTAACACTGGAAGATTTAAAGAATAAAAACTCCTGCATAAACGATTTCAGG ACTGATTTCTGTGTGGACTGAGTACATTCAGCTGACGAATTTAGTTCCCAGGAAGATGGATT GATGTTCACTAGCTTGGACAACTTCTGCAAAATATGAGACTATTTCCACTTGGGAAAAATTA СААСАССААААААААААААААААААААА

MYLSRSLSIHALWVTVSSVMQPYPLVWGHYDLCKTQIYTEEGKVWDYMACQPESTDMTKYLK
VKLDPPDITCGDPPETFCAMGNPYMCNNECDASTPELAHPPELMFDFEGRHPSTFWQSATWK
EYPKPLQVNITLSWSKTIELTDNIVITFESGRPDQMILEKSLDYGRTWQPYQYYATDCLDAF
HMDPKSVKDLSQHTVLEIICTEEYSTGYTTNSKIIHFEIKDRFALFAGPRLRNMASLYGQLD
TTKKLRDFFTVTDLRIRLLRPAVGEIFVDELHLARYFYAISDIKVRGRCKCNLHATVCVYDN
SKLTCECEHNTTGPDCGKCKKNYQGRPWSPGSYLPIPKGTANTCIPSISSIGTNVCDNELLH
CQNGGTCHNNVRCLCPAAYTGILCEKLRCEEAGSCGSDSGQGAPPHGTPALLLLTTLLGTAS
PLVF

CCCACGCGTCCGGGTGACCTGGGCCGAGCCCTCCCGGTCGGCTAAGATTGCTGAGGAGGCGG CGGGTAGCTGGCAGGCGCCGACTTCCGAAGGCCGCCGTCCGGGCGAGGTGTCCTCATGACTT $\tt CTCTTGTGGACC{\color{blue} \underline{\textbf{ATG}}} TCCGTGATCTTTTTTGCCTGCGTGGTACGGGTAAGGGATGGACTGCC$ CCTCTCAGCCTCTACTGATTTTTACCACACCCAAGATTTTTTGGAATGGAGGAGACGGCTCA AGAGTTTAGCCTTGCGACTGGCCCAGTATCCAGGTCGAGGTTCTGCAGAAGGTTGTGACTTT AGTATACATTTTTCTTCTTTCGGGGACGTGGCCTGCATGGCTATCTGCTCCTGCCAGTGTCC AGCAGCCATGGCCTTCTGCTTCCTGGAGACCCTGTGGTGGGAATTCACAGCTTCCTATGACA CTACCTGCATTGGCCTAGCCTCCAGGCCATACGCTTTTCTTGAGTTTGACAGCATCATTCAG AAAGTGAAGTGGCATTTTAACTATGTAAGTTCCTCTCAGATGGAGTGCAGCTTGGAAAAAAT TCAGGAGGAGCTCAAGTTGCAGCCTCCAGCGGTTCTCACTCTGGAGGACACAGATGTGGCAA ATGGGGTGATGAATGGTCACACCCGATGCACTTGGAGCCTGCTCCTAATTTCCGAATGGAA CCAGTGACAGCCCTGGGTATCCTCTCCCTCATTCTCAACATCATGTGTGCTGCCCTGAATCT CATTCGAGGAGTTCACCTTGCAGAACATTCTTTACAGGATCCAAGGAGCTGGTTCTGCTGGT $\tt TGGACCAAACCTCG\underline{TGA}_{GCCAGCCACCCCTGACCCAAATGAGGAGAGCTCTGATTCTCCCAT$ CCGGGAGCAGTGATGTCAAACTTCTGCTGCTGGGGAAATCTCATCAGCAGGGAGCCTGTGGA AAAGGCATGTCAGTGAAATCTGGGAATGGCTGGATTCGGAAACATCTGCCCATGTGTATTG ATGGCAGAGCTGTTGCCCACAAGCGCCTTTTATTTAGGGTAAAATTAACAAATCCATTCTAT TCCTCTGACCCATGCTTAGTACATATGACCTTTAACCCTTACATTTATATGATTCTGGGGTT GCTTCAGAAGTGTTATTTCATGAATCATTCATATGATTTGATCCCCCAGGATTCTATTTTGT TTAATGGGCTTTTCTACTAAAAGCATAAAATACTGAGGCTGATTTAGTCAGGGCAAAACCAT TTACTTTACATATTCGTTTTCAATACTTGCTGTTCATGTTACACAAGCTTCTTACGGTTTTC TTGTAACAATAAATATTTTGAGTAAATAATGGGTACATTTTAACAAACTCAGTAGTACAACC TAAACTTGTATAAAAGTGTGTAAAAATGTATAGCCATTTATATCCTATGTATAAATTAAATG AAAAG

FIGURE 76

MSVIFFACVVRVRDGLPLSASTDFYHTQDFLEWRRRLKSLALRLAQYPGRGSAEGCDFSIHF SSFGDVACMAICSCQCPAAMAFCFLETLWWEFTASYDTTCIGLASRPYAFLEFDSIIQKVKW HFNYVSSSQMECSLEKIQEELKLQPPAVLTLEDTDVANGVMNGHTPMHLEPAPNFRMEPVTA LGILSLILNIMCAALNLIRGVHLAEHSLQDPRSWFCWLDQTS

FIGURE 77

TGCTTCCTGGAGACCCTGTGGTGGGAATTCACAGCTTCNTATGACACTACCTGCATTGGCNT
AGCCTCCAGGCCATACGCTTTTCTTGAGTTTGACAGCATCATTCAGAAAGTGAAGTGGCATT
TTAACTATGTAAGTTCCTNTCAGATGGAGTGCAGCTTGGAAAAAATTCAGGAGGAGCTCAAG
TTGCAGCCTCCAGCGGTTCTCANTATGGAGGACACAGATGTGGCAAATGGGGT

CTCAGCGCGCTTCCTCGTAGCGAGCCTAGTGGCGGGTGTTTGCATTGAAACGTGAGCGCGA CCCGACCTTAAAGAGTGGGGAGCAAAGGGAGGACAGAGCCCTTTAAAACGAGGCGGGTGGTG CCTGCCCCTTTAAGGGCGGGGCGTCCGGACGACTGTATCTGAGCCCCAGACTGCCCCGAGTT TCTGTCGCAGGCTGCGAGGAAAGGCCCCTAGGCTGGGTCTGGGTGCTTGGCGGCGGCGGCTT ${\tt CCTCCCGGCTCGTCCTCCCGGGCCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGT} \underline{{\tt A}}$ **TG**GAAGCACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGC GAGTGTATTATATCAACACTTCTGTTTGCAACACTGTACATCCTCTGCCACATCTTCCTGAC CCGCTTCAAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCGTCAACAAGA TTGCGCTCGAGCTGTGCACCTTTACCCTGGCAATTGCCCTGGGTGCTGTCCTGCCCC TTCTCCATCATCAGCAATGAGGTGCTGCTCTCCCTGCCTCGGAACTACTACATCCAGTGGCT CAACGGCTCCTCATCCATGGCCTCTGGAACCTTGTTTTTCTCTTCCCCAACCTGTCCCTCA TCTTCCTCATGCCCTTTGCATATTTCTTCACTGAGTCTGAGGGCTTTGCTGGCTCCAGAAAG GGTGTCCTGGGCCGGGTCTATGAGACAGTGGTGATGTTGATGCTCCTCACTCTGCTGGTGCT AGGTATGGTGTGGGTGGCATCAGCCATTGTGGACAAGAACAAGGCCCAACAGAGAGTCACTCT CTGCTCCTGGTGTGTACTCCACTGGGTCTCGCCCGCATGTTCTCCGTCACTGGGAAGCTGCT AGTCAAGCCCCGGCTGCTGGAAGACCTGGAGGAGCAGCTGTACTGCTCAGCCTTTGAGGAGG CTACACAGACAGGTCCTGGCTCTGCAGACACAGAGGGTCCTGCTGGAGAAGAGGCGGAAGGC TTCAGCCTGGCAACGGAACCTGGGCTACCCCCTGGCTATGCTGTGCTGCTGGTGCTGACGG GCCTGTCTGTGCTCATTGTGGCCATCCACATCCTGGAGCTGCTCATCGATGAGGCTGCCATG CCCCGAGGCATGCAGGGTACCTCCTTAGGCCAGGTCTCCTTCTCCAAGCTGGGCTCCTTTGG TGCCGTCATTCAGGTTGTACTCATCTTTTACCTAATGGTGTCCTCAGTTGTGGGCTTCTATA GCTCTCCACTCTTCCGGAGCCTGCGGCCCAGATGGCACGACACTGCCATGACGCAGATAATT GGGAACTGTGTCTCTCGGTCCTAAGCTCAGCACTTCCTGTCTTCTCTCGAACCCTGGG ACTGCAGCTGTGCGGGCAGAGCTGATCCGGGCCTTTGGGCTGGACAGACTGCCGCTGCCCGT ${ t CTCCGGTTTCCCCCAGGCATCTAGGAAGACCCAGCACCAG{ t TGA}{ t CCTCCAGCTGGGGGTGGGA}}$ AGGAAAAAACTGGACACTGCCATCTGCTGCCTAGGCCTGGAGGGAAGCCCAAGGCTACTTGG ACCTCAGGACCTGGAATCTGAGAGGGTGGGTGGCAGAGGGGAGCCAGAGCCATCTGCACTATT GCATAATCTGAGCCAGAGTTTGGGACCAGGACCTCCTGCTTTTCCATACTTAACTGTGGCCT CAGCATGGGGTAGGGCTGGGTGACTGGGTCTAGCCCCTGATCCCAAATCTGTTTACACATCA ATCTGCCTCACTGCTGTTCTGGGCCATCCCCATAGCCATGTTTACATGATTTGATGTGCAAT CTTGCCTCTGGCCCAGCAGAGCCTAAGCACTGTGCTATCCTGGAGGGGCTTTGGACCACCTG AAAGACCAAGGGGATAGGGAGGAGGAGGCTTCAGCCATCAGCAATAAAGTTGATCCCAGGGA AAAAA

MEAPDYEVLSVREQLFHERIRECIISTLLFATLYILCHIFLTRFKKPAEFTTVDDEDATVNK
IALELCTFTLAIALGAVLLLPFSIISNEVLLSLPRNYYIQWLNGSLIHGLWNLVFLFPNLSL
IFLMPFAYFFTESEGFAGSRKGVLGRVYETVVMLMLLTLLVLGMVWVASAIVDKNKANRESL
YDFWEYYLPYLYSCISFLGVLLLLVCTPLGLARMFSVTGKLLVKPRLLEDLEEQLYCSAFEE
AALTRRICNPTSCWLPLDMELLHRQVLALQTQRVLLEKRRKASAWQRNLGYPLAMLCLLVLT
GLSVLIVAIHILELLIDEAAMPRGMQGTSLGQVSFSKLGSFGAVIQVVLIFYLMVSSVVGFY
SSPLFRSLRPRWHDTAMTQIIGNCVCLLVLSSALPVFSRTLGLTRFDLLGDFGRFNWLGNFY
IVFLYNAAFAGLTTLCLVKTFTAAVRAELIRAFGLDRLPLPVSGFPQASRKTQHQ

FIGURE 80

FIGURE 81

FIGURE 82

FIGURE 83

 ${\tt MLLWVILLVLAPVSGQFARTPRPIIFLQPPWTTVFQGERVTLTCKGFRFYSPQKTKWYHRYL}\\ {\tt GKEILRETPDNILEVQESGEYRCQAQGSPLSSPVHLDFSSEMGFPHAAQANVELLGSSDLLT}$

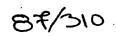


FIGURE 84

CAGAAGAGGGGCTAGCTGTCTCTGCGGACCAGGGAGACCCCGCGCCCCCCGGTGT GAGGCGGCCTCACAGGGCCGGGTGGGCTGGCGAGCCGACGCGGCGGCGGAGGAGGCTGTGAG GAGTGTGTGGAACAGGACCCGGGACAGAGGAACCATGGCTCCGCAGAACCTGAGCACCTTTT GCCTGTTGCTGCTATACCTCATCGGGGCGGTGATTGCCGGACGAGATTTCTATAAGATCTTG GGGGTGCCTCGAAGTGCCTCTATAAAGGATATTAAAAAGGCCTATAGGAAACTAGCCCTGCA GCTTCATCCCGACCGGAACCCTGATGATCCACAAGCCCAGGAGAAATTCCAGGATCTGGGTG CTGCTTATGAGGTTCTGTCAGATAGTGAGAAACGGAAACAGTACGATACTTATGGTGAAGAA GGATTAAAAGATGGTCATCAGAGCTCCCATGGAGACATTTTTTCACACTTCTTTGGGGATTT TGGTTTCATGTTTGGAGGAACCCCTCGTCAGCAAGACAGAAATATTCCAAGAGGAAGTGATA TTATTGTAGATCTAGAAGTCACTTTGGAAGAAGTATATGCAGGAAATTTTGTGGAAGTAGTT AGAAACAAACCTGTGGCAAGGCAGGCTCCTGGCAAACGGAAGTGCAATTGTCGGCAAGAGAT GCGGACCACCCAGCTGGGCCCTGGGCGCTTCCAAATGACCCAGGAGGTGGTCTGCGACGAAT GCCCTAATGTCAAACTAGTGAATGAAGAACGAACGCTGGAAGTAGAAATAGAGCCTGGGGTG AGAGACGCATGGAGTACCCCTTTATTGGAGAAGGTGAGCCTCACGTGGATGGGGAGCCTGG AGATTTACGGTTCCGAATCAAAGTTGTCAAGCACCCAATATTTGAAAGGAGAGGAGATGATT TGTACACAAATGTGACAATCTCATTAGTTGAGTCACTGGTTGGCTTTGAGATGGATATTACT CACTTGGATGGTCACAAGGTACATATTTCCCGGGATAAGATCACCAGGCCAGGAGCGAAGCT ATGGAAGAAGGGGAAGGGCTCCCCAACTTTGACAACAACAATATCAAGGGCTCTTTGATAA TCACTTTTGATGTGGATTTTCCAAAAGAACAGTTAACAGAGGAAGCGAGAGAAGGTATCAAA CAGCTACTGAAACAAGGGTCAGTGCAGAAGGTATACAATGGACTGCAAGGATAT<u>TGA</u>GAGTG TCATCATGAAATGAATAAGAGGGCTTAAGAATTTGTCCATTTGCATTCGGAAAAGAATGACC AGCAAAAGGTTTACTAATACCTCTCCCTTTGGGGATTTAATGTCTGGTGCTGCCGCCTGAGT TTCAAGAATTAAAGCTGCAAGAGGACTCCAGGAGCAAAAGAAACACAATATAGAGGGTTGGA GTTGTTAGCAATTTCATTCAAAATGCCAACTGGAGAAGTCTGTTTTTAAATACATTTTGTTG TTATTTTTA

MAPQNLSTFCLLLLYLIGAVIAGRDFYKILGVPRSASIKDIKKAYRKLALQLHPDRNPDDPQ
AQEKFQDLGAAYEVLSDSEKRKQYDTYGEEGLKDGHQSSHGDIFSHFFGDFGFMFGGTPRQQ
DRNIPRGSDIIVDLEVTLEEVYAGNFVEVVRNKPVARQAPGKRKCNCRQEMRTTQLGPGRFQ
MTQEVVCDECPNVKLVNEERTLEVEIEPGVRDGMEYPFIGEGEPHVDGEPGDLRFRIKVVKH
PIFERRGDDLYTNVTISLVESLVGFEMDITHLDGHKVHISRDKITRPGAKLWKKGEGLPNFD
NNNIKGSLIITFDVDFPKEQLTEEAREGIKQLLKQGSVQKVYNGLQGY

FIGURE 86

TGGGACCAGGGAACCCCGGGCCCCCCGGTGGAGNGCCTAACAGGCCGGTGGNTGCGACCGAA
GCGGCGGGGGGAGGAGGTTTTGAGGATTTTTGGAACAGGACCCGGACAGAGGAACCATGGTT
CCGCAGAACNTGAGCACNTTTTGCCTGTTGNTGNTATACTTCATCGGGGCGGTGATTGCCGG
ACGAGATTTNTATAAGATTTTTGGGGTGCCTNGAAGTGCCTTNTATAAAAGGATATTAAAAAAGG
CCTATAGGAAACTAGCCCTGCAGNTTTATCCCGACCGGAACCCTGATGATCCACAAGCCCAG
GAGAAATTCCAGGATTTGGGTGCTTGTTATGAGGTTNTGTCAGATAGTGAGAAACGGAAACA
GTACGATAATTATGGTGAAGAAGGATTAAAAGATGGTNATCAGAGCTCCCATGGAGACATTT
TTTCACACTTNTTTGGGGGATTTTGGTTTCATGTTTGGAGGAACCCCTNGTCAGCAAGACAGA
AATATTCCAAGAG

FIGURE 87

GGCACGAGGCGGGGGGCAGTCGCGGGATGCGCCCGGGAGCCACAGCCTGAGGCCCTCAGGT CTCTGCAGGTGTCGTGGAGGAACCTAGCACCTGCCATCCTCTTCCCCAATTTGCCACTTCCA ${\tt GCAGCTTTAGCCCATGAGGAGGATGTGACCGGGACTGAGTCAGGAGCCCTCTGGAAGC} \underline{{\tt ATG}}{\tt G}{\tt GCAGCTTTAGCCCATGAGGAGGATGTGACCGGGACTGAGTCAGGAGCCCTCTGGAAGC} \underline{{\tt ATG}}{\tt GCAGCTTTAGCCCATGAGGAGGAGCCATGAGTCAGGAGCCCTCTGGAAGC} \underline{{\tt ATG}}{\tt GCAGCTTTAGCCCATGAGGAGCCCTCTGGAAGCC} \underline{{\tt ATG}}{\tt GCAGCTTTAGCCCATGAGGAGCCCTCTGGAAGCC} \underline{{\tt ATG}}{\tt GCAGCTTTAGCCCATGAGGAGCCCTCTGGAAGCC} \underline{{\tt ATG}}{\tt GCAGCTTGAGGAGCCCTCTGGAAGCC} \underline{{\tt ATG}}{\tt GCAGCTTGAGGAGCCCTCTGGAAGCC} \underline{{\tt ATG}}{\tt GCAGCTTGAGGAGCCCTCTGGAAGCC} \underline{{\tt ATG}}{\tt GCAGCTTGAGGAGCCCTCTGGAAGCC} \underline{{\tt ATG}}{\tt GCAGCTTGAGGAGCCCTCTGGGAAGCC} \underline{{\tt ATG}}{\tt GCAGCTTGAGGAGCCCTCTGGGAAGCC} \underline{{\tt ATG}}{\tt ATG}{\tt GCAGCTTGAGGAGCCCTCTGGGAAGCC} \underline{{\tt ATG}}{\tt ATG}{\tt GCAGCTTGAGGAGCCCTCTGGGAAGCC} \underline{{\tt ATG}}{\tt ATG}{\tt AT$ AGACTGTGGTGATTGTTGCCATAGGTGTGCTGGCCACCATCTTTCTGGCTTCGTTTGCAGCC TTGGTGCTGGTTTGCAGGCAGCGCTACTGCCGGCCGCGAGACCTGCTGCAGCGCTATGATTC TAAGCCCATTGTGGACCTCATTGGTGCCATGGAGACCCAGTCTGAGCCCTCTGAGTTAGAAC TGGACGATGTCGTTATCACCAACCCCCACATTGAGGCCATTCTGGAGAATGAAGACTGGATC GAAGATGCCTCGGGTCTCATGTCCCACTGCATTGCCATCTTGAAGATTTGTCACACTCTGAC AGAGAAGCTTGTTGCCATGACAATGGGCTCTGGGGCCAAGATGAAGACTTCAGCCAGTGTCA GCGACATCATTGTGGTGGCCAAGCGGATCAGCCCCAGGGTGGATGATGTTGTGAAGTCGATG TACCCTCCGTTGGACCCCAAACTCCTGGACGCCCGGACGACTGCCCTGCTCTGTCAG TCACCTGGTGCTGGCAAGGAATGCCTGCCATCTGACGGGAGGCCTGGACTGGATTGACC AGTCTCTGTCGGCTGCTGAGGAGCATTTGGAAGTCCTTCGAGAAGCAGCCCTAGCTTCTGAG $\tt CCAGATAAAGGCCTCCCAGGCCCTGAAGGCTTCCTGCAGGAGCAGTCTGCAATT\underline{TAG}{TGCCT}$ ACAGGCCAGCAGCTAGCCATGAAGGCCCCTGCCGCCATCCCTGGATGGCTCAGCTTAGCCTT TAAAGCAGGAGATCCCCGTCAGTTTATGCCTCTTTTGCAGTTGCAAACTGTGGCTGGTGAGT GGCAGTCTAATACTACAGTTAGGGGAGATGCCATTCACTCTCTGCAAGAGGAGTATTGAAAA CTGGTGGACTGTCAGCTTTATTTAGCTCACCTAGTGTTTTCAAGAAAATTGAGCCACCGTCT AAGAAATCAAGAGGTTTCACATTAAAATTAGAATTTCTGGCCTCTCTCGATCGGTCAGAATG GGTCCCTGAGGCGTCTGGGTCTCTCCCTCTCCCTTGCAGGTTTGGGTTTGAAGCTGAGGAACT ACAAAGTTGATGATTTCTTTTTATCTTTATGCCTGCAATTTTACCTAGCTACCACTAGGTG

FIGURE 88

METVVIVAIGVLATIFLASFAALVLVCRQRYCRPRDLLQRYDSKPIVDLIGAMETQSEPSEL ELDDVVITNPHIEAILENEDWIEDASGLMSHCIAILKICHTLTEKLVAMTMGSGAKMKTSAS VSDIIVVAKRISPRVDDVVKSMYPPLDPKLLDARTTALLLSVSHLVLVTRNACHLTGGLDWI DQSLSAAEEHLEVLREAALASEPDKGLPGPEGFLQEQSAI

GCTTCATTTCTCCCGACTCAGCTTCCCACCCTGGGCTTTCCGAGGTGCTTTCGCCGCTGTCC $\tt CCACCACTGCAGCC{\color{blue} \underline{ATG}} {\color{blue} \underline{ATCTCCTTAACGGACACGCAGAAAATTGGAATGGGATTAACAGGA}$ TTTGGAGTGTTTTTCCTGTTCTTTGGAATGATTCTCTTTTTTGACAAAGCACTACTGGCTAT TCTTCTTCCAAAAACATAAAATGAAAGCTACAGGTTTTTTTCTGGGTGGTGTATTTGTAGTC ${\tt CTTATTGGTTGGCCTTTGATAGGCATGATCTTCGAAATTTATGGATTTTTTCTCTTGTTCAG}$ GGGCTTCTTTCCTGTCGTTGTTGGCTTTATTAGAAGAGTGCCAGTCCTTGGATCCCTCCTAAAT ${\tt TTACCTGGAATTAGATCATTTGTAGATAAAGTTGGAGAAAGCAACAATATGGTA\underline{{\tt TAA}}{\tt CAACA}$ GCACAAAATTAAATTACATGAAATAGCTTGTAATGTTCTTTACAGGAGTTTAAAACGTATAG CCTACAAAGTACCAGCAGCAAATTAGCAAAGAAGCAGTGAAAACAGGCTTCTACTCAAGTGA ACTAAGAAGAAGTCAGCAAGCAAACTGAGAGAGGTGAAATCCATGTTAATGATGCTTAAGAA ACTCTTGAAGGCTATTTGTGTTGTTTTTCCACAATGTGCGAAACTCAGCCATCCTTAGAGAA CTGTGGTGCCTGTTTCTTTTTTTTTTTTTTTTGAAGGCTCAGGAGCATCCATAGGCATTTGCT TTTTAGAAGTGTCCACTGCAATGGCAAAAATATTTCCAGTTGCACTGTATCTCTGGAAGTGA TGCATGAATTCGATTGGATTGTCATTTTAAAGTATTAAAACCAAGGAAACCCCAATTTTG ATGTATGGATTACTTTTTTTTGNGCNCAGGGCC

FIGURE 90

MISLTDTQKIGMGLTGFGVFFLFFGMILFFDKALLAIGNVLFVAGLAFVIGLERTFRFFFQK HKMKATGFFLGGVFVVLIGWPLIGMIFEIYGFFLLFRGFFPVVVGFIRRVPVLGSLLNLPGI RSFVDKVGESNNMV

Important features:

Transmembrane domains:

amino acids 12-30 (typeII), 33-52, 69-89 and 93-109

N-myristoylation sites.

amino acids 11-16, 51-56 and 116-121

Aminoacyl-transfer RNA synthetases class-II protein. amino acids 49-59

FIGURE 91

GGCACGAGGCTGAACCCAGCCGGCTCCATCTCAGCTTCTGGTTTCTAAGTCCATGTGCCAAA CTGTGGGTAGTTATTTATTTCTGAATAAGAGCGTCCACGCATCATGGACCTCGCGGGACTGC TGAAGTCTCAGTTCCTGTGCCACCTGGTCTTCTGCTACGTCTTTATTGCCTCAGGGCTAATC ATCAACACCATTCAGCTCTTCACTCTCCTCTCTGGCCCATTAACAAGCAGCTCTTCCGGAA GATCAACTGCAGACTGTCCTATTGCATCTCAAGCCAGCTGGTGATGCTGCTGGAGTGGTGGT GCCATCGTGGTTCTCAACCACAAGTTTGAAATTGACTTTCTGTGTGGCTGGAGCCTGTCCGA TTATCGGCTGGATGTGGTACTTCACCGAGATGGTCTTCTGTTCGCGCAAGTGGGAGCAGGAT CGCAAGACGGTTGCCACCAGTTTGCAGCACCTCCGGGACTACCCCGAGAAGTATTTTTTCCT GATTCACTGTGAGGGCACACGGTTCACGGAGAAGAAGCATGAGATCAGCATGCAGGTGGCCC GGGCCAAGGGGCTGCCTCGCCTCAAGCATCACCTGTTGCCACGAACCAAGGGCTTCGCCATC ACCGTGAGGAGCTTGAGAAATGTAGTTTCAGCTGTATATGACTGTACACTCAATTTCAGAAA TTAGGAGGATCCCACTGGAAGACATCCCTGAAGACGATGACGAGTGCTCGGCCTGGCTGCAC AAGCTCTACCAGGAGAAGGATGCCTTTCAGGAGGAGTACTACAGGACGGCACCTTCCCAGA GACGCCCATGGTGCCCCCCGGCGGCCCTGGACCCTCGTGAACTGGCTGTTTTGGGCCTCGC TGGTGCTCTACCCTTTCTTCCAGTTCCTGGTCAGCATGATCAGGAGCGGGTCTTCCCTGACG GACGGAAATTGACAAGGGCTCTGCCTACGGCAACTCTGACAGCAGCAGCAGAAACTGAATGACT **GACTCAGGGAGGTGTCACCATCCGAAGGGAACCTTGGGGAACTGGTGGCCTCTGCATATCCT** CCTTAGTGGGACACGGTGACAAAGGCTGGGTGAGCCCCTGCTGGGCACGGCGGAAGTCACGA CCTCTCCAGCCAGGGAGTCTGGTCTCAAGGCCGGATGGGGAGGAAGATGTTTTGTAATCTTT TTTTCCCCATGTGCTTTAGTGGGCTTTGGTTTTCTTTTTTGTGCGAGTGTGTGAGAATGGC TGTGTGGTGAGTGTGAACTTTGTTCTGTGATCATAGAAAGGGTATTTTAGGCTGCAGGGGAG GGCAGGGCTGGGGACCGAAGGGGACAAGTTCCCCTTTCATCCTTTGGTGCTGAGTTTTCTGT AACCCTTGGTTGCCAGAGATAAAGTGAAAAGTGCTTTAGGTGAGATGACTAAATTATGCCTC

FIGURE 93

MDLAGLLKSQFLCHLVFCYVFIASGLIINTIQLFTLLLWPINKQLFRKINCRLSYCISSQLV
MLLEWWSGTECTIFTDPRAYLKYGKENAIVVLNHKFEIDFLCGWSLSERFGLLGGSKVLAKK
ELAYVPIIGWMWYFTEMVFCSRKWEQDRKTVATSLQHLRDYPEKYFFLIHCEGTRFTEKKHE
ISMQVARAKGLPRLKHHLLPRTKGFAITVRSLRNVVSAVYDCTLNFRNNENPTLLGVLNGKK
YHADLYVRRIPLEDIPEDDDECSAWLHKLYQEKDAFQEEYYRTGTFPETPMVPPRRPWTLVN
WLFWASLVLYPFFQFLVSMIRSGSSLTLASFILVFFVASVGVRWMIGVTEIDKGSAYGNSDS
KQKLND

97/310

FIGURE 94

CTGAGGCGGCGTAGCATGGAGGGGGAGAGTACGTCGGCGGTGCTCTCGGGCTTTGTGCTCG GCGCACTCGCTTTCCAGCACCTCAACACGGACTCGGACACGGAAGGTTTTCTTCTTGGGGAA GTAAAAGGTGAAGCCAAGAACAGCATTACTGATTCCCAAATGGATGATGTTGAAGTTGTTTA TACAATTGACATTCAGAAATATATTCCATGCTATCAGCTTTTTAGCTTTTATAATTCTTCAG GCGAAGTAAATGAGCAAGCACTGAAGAAAATATTATCAAATGTCAAAAAGAATGTGGTAGGT AAACTTGCAGGAGCATTTTTCAAACCAAGACCTTGTTTTTCTGCTATTAACACCAAGTATAA TAACAGAAAGCTGCTCTACTCATCGACTGGAACATTCCTTATATAAACCTCAAAAAGGACTT TTTCACAGGGTACCTTTAGTGGTTGCCAATCTGGGCATGTCTGAACAACTGGGTTATAAAAC TGTATCAGGTTCCTGTATGTCCACTGGTTTTAGCCGAGCAGTACAAACACACAGCTCTAAAT TTTTTGAAGAAGATGGATCCTTAAAGGAGGTACATAAGATAAATGAAATGTATGCTTCATTA CAAGAGGAATTAAAGAGTATATGCAAAAAAGTGGAAGACAGTGAACAAGCAGTAGATAAACT AGTAAAGGATGTAAACAGATTAAAACGAGAAATTGAGAAAAGGAGAGGAGCACAGATTCAGG CAGCAAGAGAAGAACATCCAAAAAGACCCTCAGGAGAACATTTTTCTTTGTCAGGCATTA CGGACCTTTTTTCCAAATTCTGAATTTCTTCATTCATGTGTTATGTCTTTAAAAAATAGACA TGTTTCTAAAAGTAGCTGTAACTACAACCACCATCTCGATGTAGTAGACAATCTGACCTTAA TGGTAGAACACACTGACATTCCTGAAGCTAGTCCAGCTAGTACACCACAAATCATTAAGCAT **AAAGCCTTAGACTAGATGACAGATGGCAATTCAAGAGATCTCGGTTGTTAGATACACAAGA** CAAACGATCTAAAGCAAATACTGGTAGTAGTAACCAAGATAAAGCATCCAAAATGAGCAGCC CAGAAACAGATGAAGAATTGAAAAGATGAAGGGTTTTGGTGAATATTCACGGTCTCCTACA TTCTATTGTTTTACTATGTTGAGCTACTTGCAGTAAGTTCATTTGTTTTTACTATGTTCAC CTGTTTGCAGTAATACACAGATAACTCTTAGTGCATTTACTTCACAAAGTACTTTTTCAAAAC ATCAGATGCTTTTATTTCCAAACCTTTTTTCACCTTTCACTAAGTTGTTGAGGGGAAGGCT TACACAGACACATTCTTTAGAATTGGAAAAGTGAGACCAGGCACAGTGGCTCACACCTGTAA TGGGCAACGTATTGAGACCATGTCTATTAAAAAATAAAATGGAAAAGCAAGAATAGCCTTAT TTTCAAAATATGGAAAGAAATTTATATGAAAATTTATCTGAGTCATTAAAATTCTCCTTAAG TGATACTTTTTTAGAAGTACATTATGGCTAGAGTTGCCAGATAAAATGCTGGATATCATGCA

FIGURE 95

MEGESTSAVLSGFVLGALAFQHLNTDSDTEGFLLGEVKGEAKNSITDSQMDDVEVVYTIDIQ
KYIPCYQLFSFYNSSGEVNEQALKKILSNVKKNVVGWYKFRRHSDQIMTFRERLLHKNLQEH
FSNQDLVFLLLTPSIITESCSTHRLEHSLYKPQKGLFHRVPLVVANLGMSEQLGYKTVSGSC
MSTGFSRAVQTHSSKFFEEDGSLKEVHKINEMYASLQEELKSICKKVEDSEQAVDKLVKDVN
RLKREIEKRRGAQIQAAREKNIQKDPQENIFLCQALRTFFPNSEFLHSCVMSLKNRHVSKSS
CNYNHHLDVVDNLTLMVEHTDIPEASPASTPQIIKHKALDLDDRWQFKRSRLLDTQDKRSKA
NTGSSNQDKASKMSSPETDEEIEKMKGFGEYSRSPTF

99/310

FIGURE 96

CCGCGGCGCCTGCCACCCTTCCCTCCTTCCCCGCGTCCCCGCCTCGCCGGCCAGTCAGCTTG CCGGGTTCGCTGCCCCGCGAAACCCCGAGGTCACCAGCCCGCGCCTCTGCTTCCCTGGGCCG CGCGCCGCCTCCACGCCCTCCTTCTCCCCTGGCCCGGCGCCTGGCACCGGGGACCGTTGCCT GACGCGAGGCCCAGCTCTACTTTTCGCCCCGCGTCTCCTCCGCCTGCTCGCCTCTTCCACCA ACTCCAACTCCTTCTCCCTCCAGCTCCACTCGCTAGTCCCCGACTCCGCCAGCCCTCGGCCC GCTGCCGTAGCGCCGCTTCCCGTCCGGTCCCAAAGGTGGGAACGCGTCCGCCCCGGCCCGCA CCATGGCACGGTTCGGCTTGCCCGCGCTTCTCTGCACCCTGGCAGTGCTCAGCGCCGCGCTG CTGGCTGCCGAGCTCAAGTCGAAAAGTTGCTCGGAAGTGCGACGTCTTTACGTGTCCAAAGG CTTCAACAAGAACGATGCCCCCCTCCACGAGATCAACGGTGATCATTTGAAGATCTGTCCCC AGGGTTCTACCTGCTGCTCCAAGAGATGGAGGAGAAGTACAGCCTGCAAAGTAAAGATGAT TTCAAAAGTGTGGTCAGCGAACAGTGCAATCATTTGCAAGCTGTCTTTGCTTCACGTTACAA GAAGTTTGATGAATTCTTCAAAGAACTACTTGAAAATGCAGAGAAATCCCTGAATGATATGT TTGTGAAGACATATGGCCATTTATACATGCAAAATTCTGAGCTATTTAAAGATCTCTTCGTA GAGTTGAAACGTTACTACGTGGTGGGAAATGTGAACCTGGAAGAAATGCTAAATGACTTCTG GGCTCGCCTCCTGGAGCGGATGTTCCGCCTGGTGAACTCCCAGTACCACTTTACAGATGAGT **ATCTGGAATGTGTGAGCAAGTATACGGAGCAGCTGAAGCCCTTCGGAGATGTCCCTCGCAAA** TTGAAGCTCCAGGTTACTCGTGCTTTTGTAGCAGCCCGTACTTTCGCTCAAGGCTTAGCGGT TGCGGGAGATGTCGTGAGCAAGGTCTCCGTGGTAAACCCCACAGCCCAGTGTACCCATGCCC TGTTGAAGATGATCTACTGCTCCCACTGCCGGGGTCTCGTGACTGTGAAGCCATGTTACAAC TACTGCTCAAACATCATGAGAGGCTGTTTGGCCAACCAAGGGGATCTCGATTTTGAATGGAA CAATTTCATAGATGCTATGCTGATGGTGGCAGAGAGGCTAGAGGGTCCTTTCAACATTGAAT CGGTCATGGATCCCATCGATGTGAAGATTTCTGATGCTATTATGAACATGCAGGATAATAGT GTTCAAGTGTCTCAGAAGGTTTTCCAGGGATGTGGACCCCCCAAGCCCCTCCCAGCTGGACG AATTTCTCGTTCCATCTCTGAAAGTGCCTTCAGTGCTCGCTTCAGACCACATCACCCCGAGG AACGCCCAACCACAGCAGCTGGCACTAGTTTGGACCGACTGGTTACTGATGTCAAGGAGAAA CTGAAACAGGCCAAGAAATTCTGGTCCTCCCTTCCGAGCAACGTTTGCAACGATGAGAGGAT GGCTGCAGGAAACGGCAATGAGGATGACTGTTGGAATGGGAAAGGCAAAAGCAGGTACCTGT TTGCAGTGACAGGAAATGGATTAGCCAACCAGGGCAACAACCCAGAGGTCCAGGTTGACACC AGCAAACCAGACATACTGATCCTTCGTCAAATCATGGCTCTTCGAGTGATGACCAGCAAGAT GAAGAATGCATACAATGGGAACGACGTGGACTTCTTTGATATCAGTGATGAAAGTAGTGGAG AAGGAAGTGGAAGTGGCTGTGAGTATCAGCAGTGCCCTTCAGAGTTTGACTACAATGCCACT TCTCAAACTCTGAGAAAAAGTGTTCATCAAAAAGTTAAAAGGCACCAGTTATCACTTTTCTA CCATCCTAGTGACTTTGCTTTTTAAATGAATGGACAACAATGTACAGTTTTTACTATGTGGC CACTGGTTTAAGAAGTGCTGACTTTGTTTTCTCATTCAGTTTTGGGAGGAAAAGGGACTGTG CATTGAGTTGGTTCCTGCTCCCCAAACCATGTTAAACGTGGCTAACAGTGTAGGTACAGAA ATTTCGTTTGTGGGTTTTTTTTTCCAACTGTGATCTCGCCTTGTTTCTTACAAGCAAACCAG **GGTCCCTTCTTGGCACGTAACATGTACGTATTTCTGAAATATTAAATAGCTGTACAGAAGCA** GGTTTTATTTATCATGTTATCTTATTAAAAGAAAAAGCCCAAAAAGC . 500

FIGURE 97

MARFGLPALLCTLAVLSAALLAAELKSKSCSEVRRLYVSKGFNKNDAPLHEINGDHLKICPQ
GSTCCSQEMEEKYSLQSKDDFKSVVSEQCNHLQAVFASRYKKFDEFFKELLENAEKSLNDMF
VKTYGHLYMQNSELFKDLFVELKRYYVVGNVNLEEMLNDFWARLLERMFRLVNSQYHFTDEY
LECVSKYTEQLKPFGDVPRKLKLQVTRAFVAARTFAQGLAVAGDVVSKVSVVNPTAQCTHAL
LKMIYCSHCRGLVTVKPCYNYCSNIMRGCLANQGDLDFEWNNFIDAMLMVAERLEGPFNIES
VMDPIDVKISDAIMNMQDNSVQVSQKVFQGCGPPKPLPAGRISRSISESAFSARFRPHHPEE
RPTTAAGTSLDRLVTDVKEKLKQAKKFWSSLPSNVCNDERMAAGNGNEDDCWNGKGKSRYLF
AVTGNGLANQGNNPEVQVDTSKPDILILRQIMALRVMTSKMKNAYNGNDVDFFDISDESSGE
GSGSGCEYQQCPSEFDYNATDHAGKSANEKADSAGVRPGAQAYLLTVFCILFLVMQREWR

FIGURE 98

→102 /310 FIGURE 99

MKVLISSLLLLLPLMLMSMVSSSLNPGVARGHRDRGQASRRWLQEGGQECECKDWFLRAPRR KFMTVSGLPKKQCPCDHFKGNVKKTRHQRHHRKPNKHSRACQQFLKQCQLRSFALPL

→03/310 FIGURE 100

ANTIGORIGATION CONTROL OF THE TOTAL CONTROL ON THE TOTAL CONTROL OF THE TOTAL CONTROL OF THE TOTAL CONTROL ON THE TOTAL CONTROL OF THE TOTAL CONTROL ON THE

MAVLVLRLTVVLGLLVLFLTCYADDKPDKPDDKPDDSGKDPKPDFPKFLSLLGTEIIENAVE FILRSMSRSTGFMEFDDNEGKHSSK

GGACGCCAGCGCCTGCAGAGGCTGAGCAGGGAAAAAGCCAGTGCCCCAGCGGAAGCACAGCT CAGAGCTGGTCTGCCATGGACATCCTGGTCCCACTCCTGCAGCTGCTGGTGCTGCTTCTTAC CCTGCCCCTGCACCTCATGGCTCTGCTGGGCTGCTGGCAGCCCCTGTGCAAAAGCTACTTCC CCTACCTGATGGCCGTGCTGACTCCCAAGAGCAACCGCAAGATGGAGAGCAAGAAACGGGAG CTCTTCAGCCAGATAAAGGGGCTTACAGGAGCCTCCGGGAAAGTGGCCCTACTGGAGCTGGG CTGCGGAACCGGAGCCAACTTTCAGTTCTACCCACCGGGCTGCAGGGTCACCTGCCTAGACC CAAATCCCCACTTTGAGAAGTTCCTGACAAAGAGCATGGCTGAGAACAGGCACCTCCAATAT GGAGAGTACTGAGACCGGGAGGTGTGCTCTTTTTCTGGGAGCATGTGGCAGAACCATATGGA AGCTGGGCCTTCATGTGGCAGCAAGTTTTCGAGCCCACCTGGAAACACATTGGGGATGGCTG CTGCCTGACCAGAGAGCCTGGAAGGATCTTGAGAACGCCCAGTTCTCCGAAATCCAAATGG AACGACAGCCCCCTCCCTTGAAGTGGCTACCTGTTGGGCCCCACATCATGGGAAAGGCTGTC AAACAATCTTTCCCAAGCTCCAAGGCACTCATTTGCTCCTTCCCCAGCCTCCAATTAGAACA CATGTACCACCTACTAGTCCCTCTCTCCCCAACCTCTGCCAGGGCAATCTCTAACTTCAATC CCGCCTTCGACAGTGAAAAAGCTCTACTTCTACGCTGACCCAGGGAGGAAACACTAGGACCC TGTTGTATCCTCAACTGCAAGTTTCTGGACTAGTCTCCCAACGTTTGCCTCCCAATGTTGTC CCTTTCCTTCGTTCCCATGGTAAAGCTCCTCTCGCTTTCCTCCTGAGGCTACACCCATGCGT CTCTAGGAACTGGTCACAAAAGTCATGGTGCCTGCATCCCTGCCAAGCCCCCTGACCCTCT CTCCCACTACCACCTTCTTCCTGAGCTGGGGGCACCAGGGAGAATCAGAGATGCTGGGGAT **AACCACG**

MDILVPLLQLLVLLLTLPLHLMALLGCWQPLCKSYFPYLMAVLTPKSNRKMESKKRELFSQI KGLTGASGKVALLELGCGTGANFQFYPPGCRVTCLDPNPHFEKFLTKSMAENRHLQYERFVV APGEDMRQLADGSMDVVVCTLVLCSVQSPRKVLQEVRRVLRPGGVLFFWEHVAEPYGSWAFM WQQVFEPTWKHIGDGCCLTRETWKDLENAQFSEIQMERQPPPLKWLPVGPHIMGKAVKQSFP SSKALICSFPSLQLEQATHQPIYLPLRGT

GTGGGATTTATTTGAGTGCAAGATCGTTTTCTCAGTGGTGGTGGAAGTTGCCTCATCGCAGG CAGATGTTGGGGCTTTGTCCGAACAGCTCCCCTCTGCCAGCTTCTGTAGATAAGGGTTAAAA ACTAATATTTATATGACAGAAGAAAAAG<u>ATG</u>TCATTCCGTAAAGTAAACATCATCTTGG TCCTGGCTGTTGCTCTTCTTACTGGTTTTGCACCATAACTTCCTCAGCTTGAGCAGTTTG TTAAGGAATGAGGTTACAGATTCAGGAATTGTAGGGCCTCAACCTATAGACTTTGTCCCAAA TGCTCTCCGACATGCAGTAGATGGGAGACAAGAGGAGATTCCTGTGGTCATCGCTGCATCTG AAGACAGGCTTGGGGGGGCCATTGCAGCTATAAACAGCATTCAGCACAACACTCGCTCCAAT GTGATTTTCTACATTGTTACTCTCAACAATACAGCAGACCATCTCCGGTCCTGGCTCAACAG AAGTAAAGGAGGATCCTGACCAGGGGGAATCCATGAAACCTTTAACCTTTGCAAGGTTCTAC TTGCCAATTCTGGTTCCCAGCGCAAAGAAGGCCATATACATGGATGATGATGTAATTGTGCA AGGTGATATTCTTGCCCTTTACAATACAGCACTGAAGCCAGGACATGCAGCTGCATTTTCAG AAGATTGTGATTCAGCCTCTACTAAAGTTGTCATCCGTGGAGCAGGAAACCAGTACAATTAC **ATTGGCTATCTTGACTATAAAAAGGAAAGAATTCGTAAGCTTTCCATGAAAGCCAGCACTTG** CTCATTTAATCCTGGAGTTTTTGTTGCAAACCTGACGGAATGGAAACGACAGAATATAACTA ACCAACTGGAAAAATGGATGAAACTCAATGTAGAAGAGGGACTGTATAGCAGAACCCTGGCT GGTAGCATCACAACACCTCCTCTGCTTATCGTATTTTATCAACAGCACTCTACCATCGATCC TATGTGGAATGTCCGCCACCTTGGTTCCAGTGCTGGAAAACGATATTCACCTCAGTTTGTAA AGGCTGCCAAGTTACTCCATTGGAATGGACATTTGAAGCCATGGGGAAGGACTGCTTCATAT ACTGATGTTTGGGAAAAATGGTATATTCCAGACCCAACAGGCAAATTCAACCTAATCCGAAG ATATACCGAGATCTCAAACATAAAG<u>TGA</u>AACAGAATTTGAACTGTAAGCAAGCATTTCTCAG GAAGTCCTGGAAGATAGCATGCATGGGAAGTAACAGTTGCTAGGCTTCAATGCCTATCGGTA GCAAGCCATGGAAAAAGATGTCTCAGCTAGGTAAAGATGACAAACTGCCCTGTCTGGCAGTC AGCTTCCCAGACAGACTATAGACTATAAATATGTCTCCATCTGCCTTACCAAGTGTTTTCTT ACATTTTTC

108/340 FIGURE 105

MSFRKVNIIILVLAVALFILVLHHNFLSLSSLLRNEVTDSGIVGPQPIDFVPNALRHAVDGR QEEIPVVIAASEDRLGGAIAAINSIQHNTRSNVIFYIVTLNNTADHLRSWLNSDSLKSIRYK IVNFDPKLLEGKVKEDPDQGESMKPLTFARFYLPILVPSAKKAIYMDDDVIVQGDILALYNT ALKPGHAAAFSEDCDSASTKVVIRGAGNQYNYIGYLDYKKERIRKLSMKASTCSFNPGVFVA NLTEWKRQNITNQLEKWMKLNVEEGLYSRTLAGSITTPPLLIVFYQQHSTIDPMWNVRHLGS SAGKRYSPQFVKAAKLLHWNGHLKPWGRTASYTDVWEKWYIPDPTGKFNLIRRYTEISNIK

_____/310 FIGURE 107

TGGGCTCCGGGGCCTGCGGCGGCGGCTGAGCTGGCAGGCGGGCTCGGGGCGCGGCTGCA TCCGCATCTCCTCCATCGCCTGCAGTAAGGGCGGCCGCGGCGAGCCTTTGAGGGGAACGACT TGTCGGAGCCCTAACCAGGGGTGTCTCTGAGCCTGGTGGGATCCCCGGAGCGTCACATCACT TTCCGATCACTTCAAAGTGGTTAAAAACTAATATTTATATGACAGAAGAAAAAGATGTCATT CCGTAAAGTAAACATCATCATCTTGGTCCTGGGCTGTTGCTCTCTTACTGGTTTTTGCAC CATAACTTCCTCAGCTTGAGGCAGTTTGTTAAGGAATGAGGTTACAGATTCAGGAATTGTAG GGCCTCAACCTATAGGACTTTGTCCCAAATGCTCTCCGACATGCAGTAGATGGGAGACAAGA GGAGATTCCTGTGGTCATCGCTGCATCTGAAGACAGGCTTGGGGGGGCCCATTGCAGCTATAA ACAGCATTCAGCACAACACTCGCTCCAATGTGATTTTCTACATTGTTACTCTCAACAATACA GCAGACCATCTCCGGTCCTGGGCTCAACAGTGATTCCCTGAAAAGCATCAGATACAAAATTG TCAATTTTGACCCTAAACTTTTGGAAGGAAAAGTAAAGGAGGATCCTGACCAGGGGAATCC ATGAAACCTTTAACCTTTGCAAGGTTCTACTTGCCAATTCTGGGTTCCCAGCGCAAAGAAGG CCATATACATGGATGATGTAATTGTGCAAGGTGATATTCTTGCCCTTTACAATACAGCA CTGAAGCCAGGACATGCAGCTGCATTTTCAGAAGATTGTGATTCAGCCTCTACTAAAGTTGT CATCCGTGGAGCAGGAAACCAGTACAATTACATTGGCTATCTTGACTATAAAAAGGAAAGAA TTCGTAAGCTTTCCATGAAAGCCAGCACTTGCTCATTTAATCCTGGAGTTTTTGTTGCAAAC CTGACGGAATGGAAACGACAGAATATAACTAACCAACTGGAAAAATGGATGAAACTCAATGT AGAAGAGGGACTGTATAGCAGAACCCTGGCTGGTAGCATCACAACACCTCCTCTGCTTATCG TATTTTATCAACAGCACTCTACCATCGATCCTATGTGGAATGTCCGCCACCTTGGTTCCAGT GCTGGAAAACGATATTCACCTCAGTTTGTAAAGGCTGCCAAGTTACTCCATTGGAATGGACA TTTGAAGCCATGGGGAAGGACTGCTTCATATACTGATGTTTGGGGAAAAATGGTATATTCCA GACCCAACAGGCAAATTCAACCTAATCCGAAGATATACCGAGATCTCAAACATAAAGTGAAA CAGAATTTGAACTGTAAGCAAGCATTTCTCAGGAAGTCCTGGAAGATAGCATGCGTGGGAAG TAACAGTTGCTAGGCTTCAATGCCTATCGGTAGCAAGCCATGGAAAAAGATGTGTCAGCTAG ATGTCTCCATCTGCCTTACCAAGTGTTTTCTTACTACAATGCTGAATGACTGGAAAGAAGAA CTGATATGGCTAGTTCAGCTAGCTGGTACAGATAATTCAAAACTGCTGTTGGTTTTAATTTT AAAAA

PCT/US99/12252

1-12 /310 FIGURE 109

MGAAISQGALIAIVCNGLVGFLLLLLWVILCWACHSRLPTLTLSLNPVPTPALAPVLRRPHH PRSPAMKAATCCSPEGPWPSLEPRT

~13/510 FIGURE 110

GTTTGAATTCCTTCAACTATACCCACAGTCCAAAAGCAGACTCACTGTGTCCCAGGCTACCA GTTCCTCCAAGCAAGTCATTTCCCTTATTTAACCGATGTGTCCCTCAAACACCTGAGTGCTA CTCCCTATTTGCATCTGTTTTGATAAATGATGTTGACACCCTCCACCGAATTCTAAGTGGAA ${\tt TC}{\tt \underline{ATG}}{\tt TCGGGAAGAGATACAATCCTTGGCCTGTGTATCCTCGCATTAGCCTTGTCTTTGGCC}$ ATGATGTTTACCTTCAGATTCATCACCACCCTTCTGGTTCACATTTTCATTTCATTTGGTTAT TTTGGGATTGTTGTTTGTCTGCGGTGTTTTATGGTGGCTGTATTATGACTATACCAACGACC TCCACAGGCATCACGGCAGTGCTGCTCGTCTTGATTTTTGTTCTCAGAAAGAGAATAAAATT GACAGTTGAGCTTTTCCAAATCACAAATAAAGCCATCAGCAGTGCTCCCTTCCTGCTGTTCC AGCCACTGTGGACATTTGCCATCCTCATTTTCTTCTGGGTCCTCTGGGTGGCTGCTGCTG AGCCTGGGAACTGCAGGAGCTGCCCAGGTTATGGAAGGCGGCCAAGTGGAATATAAGCCCCT TTCGGGCATTCGGTACATGTGGTCGTACCATTTAATTGGCCTCATCTGGACTAGTGAATTCA TCCTTGCGTGCCAGCAAATGACTATAGCTGGGGCAGTGGTTACTTGTTATTTCAACAGAAGT AAAAATGATCCTGATCATCCCATCCTTTCGTCTCTCTCCCATTCTTCTTCTACCATCA AGGAACCGTTGTGAAAGGGTCATTTTTAATCTCTGTGGTGAGGATTCCGAGAATCATTGTCA TGTACATGCAAAACGCACTGAAAGAACAGCAGCATGGTGCATTGTCCAGGTACCTGTTCCGA TGCTGCTACTGCTGTTTCTGGTGTCTTGACAAATACCTGCTCCATCTCAACCAGAATGCATA TACTACAACTGCTATTAATGGGACAGATTTCTGTACATCAGCAAAAGATGCATTCAAAATCT TGTCCAAGAACTCAAGTCACTTTACATCTATTAACTGCTTTGGAGACTTCATAATTTTTCTA GGAAAGGTGTTAGTGGTGTTTTCACTGTTTTTGGAGGACTCATGGCTTTTAACTACAATCG ATAGTTTTTTATCTGTGTTTGAAACTGTGCTGGATGCACTTTTCCTGTGTTTTGCTGTTTGAT CTGGAAACAAATGATGGATCGTCAGAAAAGCCCTACTTTATGGATCAAGAATTTCTGAGTTT CGTAAAAAGGAGCAACAAATTAAACAATGCAAGGGCACAGCAGGACAAGCACTCATTAAGGA ${\tt ATGAGGAGGGAACAGAACTCCAGGCCATTGTGAGA\underline{TAG}ATACCCATTTAGGTATCTGTACCT}$ GGAAAACATTTCCTTCTAAGAGCCATTTACAGAATAGAAGATGAGACCACTAGAGAAAAGTT AGTGAATTTTTTTTAAAAGACCTAATAAACCCTATTCTTCCTCAAAA

-14/310 FIGURE 111

MSGRDTILGLCILALALSLAMMFTFRFITTLLVHIFISLVILGLLFVCGVLWWLYYDYTNDL
SIELDTERENMKCVLGFAIVSTGITAVLLVLIFVLRKRIKLTVELFQITNKAISSAPFLLFQ
PLWTFAILIFFWVLWVAVLLSLGTAGAAQVMEGGQVEYKPLSGIRYMWSYHLIGLIWTSEFI
LACQQMTIAGAVVTCYFNRSKNDPPDHPILSSLSILFFYHQGTVVKGSFLISVVRIPRIIVM
YMQNALKEQQHGALSRYLFRCCYCCFWCLDKYLLHLNQNAYTTTAINGTDFCTSAKDAFKIL
SKNSSHFTSINCFGDFIIFLGKVLVVCFTVFGGLMAFNYNRAFQVWAVPLLLVAFFAYLVAH
SFLSVFETVLDALFLCFAVDLETNDGSSEKPYFMDQEFLSFVKRSNKLNNARAQQDKHSLRN
EEGTELQAIVR

 ${\tt GTTCGATTAGCTCCTCTGAGAAGAAGAGAAAAGGTTCTTGGACCTCTCCCTGTTTCTTCCTT}$ TGTGGTGAAAATTTTTTGAAAAAAAATTGCCTTCTTCAAACAAGGGTGTCATTCTGATATT $\mathtt{T}\underline{\mathtt{ATG}}\mathtt{AGGACTGTTGTTCTCACTATGAAGGCATCTGTTATTGAAATGTTCCTTGTTTTGCTGG}$ TGACTGGAGTACATTCAAACAAAGAAACGGCAAAGAAGATTAAAAGGCCCAAGTTCACTGTG CCTCAGATCAACTGCGATGTCAAAGCCGGAAAGATCATCGATCCTGAGTTCATTGTGAAATG TCCAGCAGGATGCCAAGACCCCAAATACCATGTTTATGGCACTGACGTGTATGCATCCTACT CCAGTGTGTGTGGCGCTGCCGTACACAGTGGTGTGCTTGATAATTCAGGAGGGAAAATACTT GTTCGGAAGGTTGCTGGACAGTCTGGTTACAAAGGGAGTTATTCCAACGGTGTCCAATCGTT ATCCCTACCACGATGGAGAGATCCTTTATCGTCTTAGAAAGTAAACCCAAAAAGGGTGTAA CCTACCCATCAGCTCTTACATACTCATCATCGAAAAGTCCAGCTGCCCAAGCAGGTGAGACC ACAAAAGCCTATCAGAGGCCACCTATTCCAGGGACAACTGCACAGCCGGTCACTCTGATGCA GCTTCTGGCTGTCACTGTAGCTGTGGCCACCCCCACCACCTTGCCAAGGCCATCCCCTTCTG CTGCTTCTACCACCAGCATCCCCAGACCACAATCAGTGGGCCACAGGAGCCAGGAGATGGAT CTCTGGTCCACTGCCACCTACACAAGCAGCCAAAACAGGCCCAGAGCTGATCCAGGTATCCA AAGGCAAGATCCTTCAGGAGCTGCCTTCCAGAAACCTGTTGGAGCGGATGTCAGCCTGGGAC TTGTTCCAAAAGAAGAATTGAGCACACAGTCTTTGGAGCCAGTATCCCTGGGAGATCCAAAC TGCAAAATTGACTTGTCGTTTTTAATTGATGGGAGCACCAGCATTGGCAAACGGCGATTCCG AATCCAGAAGCAGCTCCTGGCTGATGTTGCCCAAGCTCTTGACATTGGCCCTGCCGGTCCAC AATTCTCGAGATCTGAAGACAGCCATAGAGAAAATTACTCAGAGAGGAGGACTTTCTAATGT AGGTCGGGCCATCTCCTTTGTGACCAAGAACTTCTTTTCCAAAGCCAATGGAAACAGAAGCG GGGCTCCCAATGTGGTGGTGGTGGTGGATGGCTGGCCCACGGACAAAGTGGAGGAGGCT TCAAGACTTGCGAGAGAGTCAGGAATCAACATTTTCTTCATCACCATTGAAGGTGCTGCTGA AAATGAGAAGCAGTATGTGGTGGAGCCCAACTTTGCAAACAAGGCCGTGTGCAGAACAAACG GCTTCTACTCGCTCCACGTGCAGAGCTGGTTTGGCCTCCACAAGACCCTGCAGCCTCTGGTG AAGCGGGTCTGCGACACTGACCGCCTGGCCTGCAGCAAGACCTGCTTGAACTCGGCTGACAT TGGCTTCGTCATCGACGGCTCCAGCAGTGTGGGGACGGCCAACTTCCGCACCGTCCTCCAGT TTGTGACCAACCTCACCAAAGAGTTTGAGATTTCCGACACGGACACGCGCATCGGGGCCGTG CAGTACACCTACGAACAGCGGCTGGAGTTTGGGTTCGACAAGTACAGCAGCAAGCCTGACAT CCTCAACGCCATCAAGAGGGTGGGCTACTGGAGTGGTGGCACCAGCACGGGGGCTGCCATCA ACTTCGCCCTGGAGCAGCTCTTCAAGAAGTCCAAGCCCAACAAGAGGAAGTTAATGATCCTC ATCACCGACGGGAGGTCCTACGACGACGTCCGGATCCCAGCCATGGCTGCCCATCTGAAGGG AGTGATCACCTATGCGATAGGCGTTGCCTGGGCTGCCCAAGAGGAGCTAGAAGTCATTGCCA CTCACCCCGCCAGAGACCACTCCTTCTTTGTGGACGAGTTTGACAACCTCCATCAGTATGTC CCCAGGATCATCCAGAACATTTGTACAGAGTTCAACTCACAGCCTCGGAAC<u>TGA</u>ATTCAGAG CAGGCAGAGCACCAGCAAGTGCTGCTTTACTAACTGACGTGTTGGACCACCCCCACCGCTTAA TGGGGCACGCACGTGCATCAAGTCTTGGGCAGGCATGGAGAAACAAATGTCTTGTTATTA TTCTTTGCCATCATGCTTTTTCATATTCCAAAACTTGGAGTTACAAAGATGATCACAAACGT ATAGAATGAGCCAAAAGGCTACATCATGTTGAGGGTGCTGGAGATTTTACATTTTGACAATT GTTTTCAAAATAAATGTTCGGAATACAGTGCAGCCCTTACGACAGGCTTACGTAGAGCTTTT GTGAGATTTTTAAGTTGTTATTTCTGATTTGAACTCTGTAACCCTCAGCAAGTTTCATTTTT

115/310

FIGURE 113

MRTVVLTMKASVIEMFLVLLVTGVHSNKETAKKIKRPKFTVPQINCDVKAGKIIDPEFIVKC
PAGCQDPKYHVYGTDVYASYSSVCGAAVHSGVLDNSGGKILVRKVAGQSGYKGSYSNGVQSL
SLPRWRESFIVLESKPKKGVTYPSALTYSSSKSPAAQAGETTKAYQRPPIPGTTAQPVTLMQ
LLAVTVAVATPTTLPRPSPSAASTTSIPRPQSVGHRSQEMDLWSTATYTSSQNRPRADPGIQ
RQDPSGAAFQKPVGADVSLGLVPKEELSTQSLEPVSLGDPNCKIDLSFLIDGSTSIGKRRFR
IQKQLLADVAQALDIGPAGPLMGVVQYGDNPATHFNLKTHTNSRDLKTAIEKITQRGGLSNV
GRAISFVTKNFFSKANGNRSGAPNVVVMVDGWPTDKVEEASRLARESGINIFFITIEGAAE
NEKQYVVEPNFANKAVCRTNGFYSLHVQSWFGLHKTLQPLVKRVCDTDRLACSKTCLNSADI
GFVIDGSSSVGTGNFRTVLQFVTNLTKEFEISDTDTRIGAVQYTYEQRLEFGFDKYSSKPDI
LNAIKRVGYWSGGTSTGAAINFALEQLFKKSKPNKRKLMILITDGRSYDDVRIPAMAAHLKG
VITYAIGVAWAAQEELEVIATHPARDHSFFVDEFDNLHQYVPRIIQNICTEFNSQPRN

CAGGATGAACTGGTTGCAGTGGCTGCTGCTGCGGGGGCGCTGAGAGGACACGAGCTCT<u>A</u> $\underline{\textbf{TG}}\texttt{CCTTTCCGGCTGCTCATCCCGCTCGGCCTCCTGTGCGCGCTGCTGCCTCAGCACCATGGT}$ GCGCCAGGTCCCGACGGCTCCGCCCAGATCCCGCCCACTACAGTTTTTCTCTGACTCTAAT TGATGCACTGGACACCTTGCTGATTTTGGGGAATGTCTCAGAATTCCAAAGAGTGGTTGAAG CGAGTGGTAGGAGGACTCCTGTCTGCTCATCTGCTCCCAAGAAGGCTGGGGTGGAAGTAGA GGCTGGATGGCCCTGTTCCGGGCCTCTCCTGAGAATGGCTGAGGAGGCGGCCCGAAAACTCC AACCCAGGAGAGACCCCTGTCACCTGTACGGCAGGGATTGGGACCTTCATTGTTGAATTTGC CACCCTGAGCAGCCTCACTGGTGACCCGGTGTTCGAAGATGTGGCCAGAGTGGCTTTGATGC GCCTCTGGGAGAGCCGGTCAGATATCGGGCTGGTCGGCAACCACATTGATGTGCTCACTGGC AAGTGGGTGGCCCAGGACGCAGGCATCGGGGCTGGCGTGGACTCCTACTTTGAGTACTTGGT GAAAGGAGCCATCCTGCTTCAGGATAAGAAGCTCATGGCCATGTTCCTAGAGTATAACAAAG CCATCCGGAACTACACCCGCTTCGATGACTGGTACCTGTGGGTTCAGATGTACAAGGGGACT ${\tt GTGTCCATGCCAGTCTTGGAGGCCTACTGGCCTGGTCTTCAGAGCCTCATTGG}$ AGACATTGACAATGCCATGAGGACCTTCCTCAACTACTACACTGTATGGAAGCAGTTTGGGG GGCTCCCGGAATTCTACAACATTCCTCAGGGATACACAGTGGAGAAGCGAGAGGGCTACCCA CTTCGGCCAGAACTTATTGAAAGCGCAATGTACCTCTACCGTGCCACGGGGGATCCCACCCT CCTAGAACTCGGAAGAGATGCTGTGGAATCCATTGAAAAAATCAGCAAGGTGGAGTGCGGAT TTGCAACAATCAAAGATCTGCGAGACCACAAGCTGGACAACCGCATGGAGTCGTTCTTCCTG GTCCACCTTCGACGCGGTGATCACCCCCTATGGGGAGTGCATCCTGGGGGGGTACA TCTTCAACACAGAAGCTCACCCCATCGACCTTGCCGCCCTGCACTGCTGCCAGAGGCTGAAG GAAGAGCAGTGGGAGGACTTGATGAGGGAATTCTACTCTCAAACGGAGCAGGTC GAAATTTCAGAAAAACACTGTTAGTTCGGGGCCATGGGAACCTCCAGCAAGGCCAGGAACAC TCTTCTCACCAGAAAACCATGACCAGGCAAGGGAAGGCAAGCCTGCCAAACAGAAGGTCCCA $\tt CTTCTCAGCTGCCCCAGTCAGCCCTTCACCTCCAAGTTGGCATTACTGGGACAGGTTTTCCT$ $AGACTCCTCA\underline{TAA}CCACTGGATAATTTTTTTTTTTTTTTTTTTTTTTTGAGGCTAAACTATAATA$ AATTGCTTTTGGCTATCATAAAA

MPFRLLIPLGLLCALLPQHHGAPGPDGSAPDPAHYSFSLTLIDALDTLLILGNVSEFQRVVE
VLQDSVDFDIDVNASVFETNIRVVGGLLSAHLLSKKAGVEVEAGWPCSGPLLRMAEEAARKL
LPAFQTPTGMPYGTVNLLHGVNPGETPVTCTAGIGTFIVEFATLSSLTGDPVFEDVARVALM
RLWESRSDIGLVGNHIDVLTGKWVAQDAGIGAGVDSYFEYLVKGAILLQDKKLMAMFLEYNK
AIRNYTRFDDWYLWVQMYKGTVSMPVFQSLEAYWPGLQSLIGDIDNAMRTFLNYYTVWKQFG
GLPEFYNIPQGYTVEKREGYPLRPELIESAMYLYRATGDPTLLELGRDAVESIEKISKVECG
FATIKDLRDHKLDNRMESFFLAETVKYLYLLFDPTNFIHNNGSTFDAVITPYGECILGAGGY
IFNTEAHPIDLAALHCCQRLKEEQWEVEDLMREFYSLKRSRSKFQKNTVSSGPWEPPARPGT
LFSPENHDQARERKPAKQKVPLLSCPSQPFTSKLALLGQVFLDSS

AAAGTTACATTTTCTCTGGAACTCTCCTAGGCCACTCCCTGCTGATGCAACATCTGGGTTTG GGCAGAAAGGAGGGTGCTTCGGAGCCCGCCCTTTCTGAGCTTCCTGGGCCGGCTCTAGAACA GAGATGGACAGAATGCTTTATTTTGGAAAGAAACAATGTTCTAGGTCAAACTGAGTCTACCA AATGCAGACTTTCACAATGGTTCTAGAAGAAATCTGGACAAGTCTTTTCATGTGGTTTTTCT TCTGTACTCTCAACCAACATGAAGCATCTCTTGATGTGGAGCCCAGTGATCGCGCCTGGAGA **AACAGTGTACTATTCTGTCGAATACCAGGGGGAGTACGAGAGCCTGTACACGAGCCACATCT** GGATCCCCAGCAGCTGGTGCTCACTCACTGAAGGTCCTGAGTGTGATGTCACTGATGACATC ACGGCCACTGTGCCATACAACCTTCGTGTCAGGGCCACATTGGGCTCACAGACCTCAGCCTG GAGCATCCTGAAGCATCCCTTTAATAGAAACTCAACCATCCTTACCCGACCTGGGATGGAGA TCACCAAAGATGGCTTCCACCTGGTTATTGAGCTGGAGGACCTGGGGCCCCAGTTTGAGTTC CTTGTGGCCTACTGGAGGAGGGAGCCTGGTGCCGAGGAACATGTCAAAATGGTGAGGAGTGG GGGTATTCCAGTGCACCTAGAAACCATGGAGCCAGGGGCTGCATACTGTGTGAAGGCCCAGA GGAGAGGCCATTCCCCTGGTACTGGCCCTGTTTGCCTTTGTTGGCTTCATGCTGATCCTTGT GGTCGTGCCACTGTTCGTCTGGAAAATGGGCCGGCTGCTCCAGTACTCCTGTTGCCCCGTGG TGGTCCTCCCAGACACCTTGAAAATAACCAATTCACCCCAGAAGTTAATCAGCTGCAGAAGG GAGGAGGTGGATGCCTGTGCCACGGCTGTGATGTCTCCTGAGGAACTCCTCAGGGCCTGGAT CTCA<u>TAG</u>GTTTGCGGAAGGCCCAGGTGAAGCCGAGAACCTGGTCTGCATGACATGGAAACC ATGAGGGGACAAGTTGTGTTTCTGTTTTCCGCCACGGACAAGGGATGAGAAGTAGGAAGA GCCTGTTGTCTACAAGTCTAGAAGCAACCATCAGAGGCAGGGTGGTTTGTCTAACAGAACAC CTGGGAAAAGTGACTTCATCCCTTCGGTCCTAAGTTTTCTCATCTGTAATGGGGGAATTACC TGTTTCTGGAGAGCAGACATAAATGTATGATGAGAATGATCAAGGACTCTACACACTGGGT GGCTTGGAGAGCCCACTTTCCCAGAATAATCCTTGAGAGAAAAGGAATCATGGGAGCAATGG TGTTGAGTTCACTTCAAGCCCAATGCCGGTGCAGAGGGGGAATGGCTTAGCGAGCTCTACAGT AGGTGACCTGGAGGAAGGTCACAGCCACACTGAAAATGGGATGTGCATGAACACGGAGGATC TGTTGGTAAAGTACAGAATTCAGCAAATAAAAAGGGCCACCCTGGCCAAAAGCGGTAAAAA AAAAAAAAA

MQTFTMVLEEIWTSLFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGE
TVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAW
SILKHPFNRNSTILTRPGMEITKDGFHLVIELEDLGPQFEFLVAYWRREPGAEEHVKMVRSG
GIPVHLETMEPGAAYCVKAQTFVKAIGRYSAFSQTECVEVQGEAIPLVLALFAFVGFMLILV
VVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS

Important features: Signal peptide: amino acids 1-29

Transmembrane domain: amino acids 230-255

N-glycosylation sites.
amino acids 40-43 and 134-137

Tissue factor proteins homology.
amino acids 92-119

Integrins alpha chain protein homology.
amino acids 232-262

121/310

FIGURE 118

GCTGCTCCTGTGGGCTGCGCCTGCGCGCAGCAGCAGGACTTCTACGACTTCAAGGCGG TCAACATCCGGGGCAAACTGGTGTCGCTGGAGAAGTACCGCGGATCGGTGTCCCTGGTGGTG AATGTGGCCAGCGAGTGCGGCTTCACAGACCAGCACTACCGAGCCCTGCAGCAGCTGCAGCG AGACCTGGGCCCCCACCACTTTAACGTGCTCGCCTTCCCCTGCAACCAGTTTGGCCAACAGG AGCCTGACAGCAACAAGGAGATTGAGAGCTTTGCCCGCCGCACCTACAGTGTCTCATTCCCC ATGTTTAGCAAGATTGCAGTCACCGGTACTGGTGCCCATCCTGCCTTCAAGTACCTGGCCCA GACTTCTGGGAAGGAGCCCACCTGGAACTTCTGGAAGTACCTAGTAGCCCCAGATGGAAAGG TGGTAGGGGCTTGGGACCCAACTGTGTCAGTGGAGGAGGTCAGACCCCAGATCACAGCGCTC GTGAGGAAGCTCATCCTACTGAAGCGAGAAGACTTA<u>TAA</u>CCACCGCGTCTCCTCCTCCACCA CCTCATCCCGCCCACCTGTGTGGGGCTGACCAATGCAAACTCAAATGGTGCTTCAAAGGGAG AGACCCACTGACTCTCCTTTACTCTTATGCCATTGGTCCCATCATTCTTGTGGGGGAA AAATTCTAGTATTTTGATTATTTGAATCTTACAGCAACAAATAGGAACTCCTGGCCAATGAG AGCTCTTGACCAGTGAATCACCAGCCGATACGAACGTCTTGCCAACAAAAATGTGTGGCAAA TAGAAGTATATCAAGCAATAATCTCCCACCCAAGGCTTCTGTAAACTGGGACCAATGATTAC CTCATAGGGCTGTTGTGAGGATTAGGATGAAATACCTGTGAAAGTGCCTAGGCAGTGCCAGC CAAATAGGAGGCATTCAATGAACATTTTTTGCATATAAACCAAAAAATAACTTGTTATCAAT AAAAACTTGCATCCAACATGAATTTCCAGCCGATGATAATCCAGGCCAAAGGTTTAGTTGTT GTTATTTCCTCTGTATTATTTTCTTCATTACAAAAGAAATGCAAGTTCATTGTAACAATCCA AACAATACCTCACGATATAAAATAAAAATGAAAGTATCCTCCTCAAAAA

MVAATVAAAWLLLWAAACAQQEQDFYDFKAVNIRGKLVSLEKYRGSVSLVVNVASECGFTDQ HYRALQQLQRDLGPHHFNVLAFPCNQFGQQEPDSNKEIESFARRTYSVSFPMFSKIAVTGTG AHPAFKYLAQTSGKEPTWNFWKYLVAPDGKVVGAWDPTVSVEEVRPQITALVRKLILLKREDL

124/510 FIGURE 121

CGGACGCGTGGGCGGGCCGGGACGCAGGGCAAAGCGAGCC<u>ATG</u>GCTGTCTACGTCGGGATGC TGCGCCTGGGGAGGCTGTGCGCCGGGAGCTCGGGGGTGCTGGGGGGCCCGGGCCCCTCTCT CGGAGTTGGCAGGAAGCCAGGTTGCAGGGTGTCCGCTTCCTCAGTTCCAGAGAGGTGGATCG CATGGTCTCCACGCCCATCGGAGGCCTCAGCTACGTTCAGGGGTGCACCAAAAAGCATCTTA ACAGCAAGACTGTGGGCCAGTGCCTGGAGACCACAGCACAGAGGGTCCCAGAACGAGAGGCC TTGGTCGTCCTCCATGAAGACGTCAGGTTGACCTTTGCCCCAACTCAAGGAGGAGGTGGACAA AGCTGCTTCTGGCCTCCTGAGCATTGGCCTCTGCAAAGGTGACCGGCTGGGCATGTGGGGAC CTAACTCCTATGCATGGGTGCTCATGCAGTTGGCCACCGCCCAGGCGGGCATCATTCTGGTG TCTGTGAACCCAGCCTACCAGGCTATGGAACTGGAGTATGTCCTCAAGAAGGTGGGCTGCAA GGCCCTTGTGTTCCCCCAAGCAATTCAAGACCCAGCAATACTACAACGTCCTGAAGCAGATCT GTCCAGAAGTGGAGAATGCCCAGCCAGGGGCCTTGAAGAGTCAGAGGCTCCCAGATCTGACC ACAGTCATCTCGGTGGATGCCCCTTTGCCGGGGACCCTGCTCCTGGATGAAGTGGTGGCGGC TGGCAGCACGCCAGCATCTGGACCAGCTCCAATACAACCAGCAGTTCCTGTCCTGCCATG ACCCCATCAACATCCAGTTCACCTCGGGGACAACAGGCAGCCCCAAGGGGGCCCACCCTCTCC CACTACAACATTGTCAACAACTCCAACATTTTAGGAGAGCGCCTGAAACTGCATGAGAAGAC ACCAGAGCAGTTGCGGATGATCCTGCCCAACCCCCTGTACCATTGCCTGGGTTCCGTGGCAG GCACAATGATGTCTGATGTACGGTGCCACCCTCATCCTGGCCTCTCCCATCTTCAATGGC AAGAAGGCACTGGAGGCCATCAGCAGAGAGAGAGGCACCTTCCTGTATGGTACCCCCACGAT GTTCGTGGACATTCTGAACCAGCCAGACTTCTCCAGTTATGACATCTCGACCATGTGTGGAG GTGTCATTGCTGGGTCCCCTGCACCTCCAGAGTTGATCCGAGCCATCATCAACAAGATAAAT ATGAAGGACCTGGTGGTTGCTTATGGAACCACAGAGAACAGTCCCGTGACATTCGCGCACTT CCCTGAGGACACTGTGGAGCAGAAGGCAGAAAGCGTGGGCAGAATTATGCCTCACACGGAGG CCCGGATCATGAACATGGAGGCAGGGACGCTGGCAAAGCTGAACACGCCCGGGGAGCTGTGC ATCCGAGGGTACTGCGTCATGCTGGGCTACTGGGGTGAGCCTCAGAAGACAGAGGAAGCAGT AGATCGTGGGCCGCTCTAAGGATATGATCATCCGGGGTGGTGAGAACATCTACCCCGCAGAG CTCGAGGACTTCTTTCACACACACCCGAAGGTGCAGGAAGTGCAGGTGGTGGGAGTGAAGGA CGATCGGATGGGGGAAGAGATTTGTGCCTGCATTCGGCTGAAGGACGGGGAGGAGACCACGG TGGAGGÀGATAAAAGCTTTCTGCAAAGGGAAGATCTCTCACTTCAAGATTCCGAAGTACATC GTGTTTGTCACAAACTACCCCCTCACCATTTCAGGAAAGATCCAGAAATTCAAACTTCGAGA GCAGATGGAACGACATCTAAATCTG<u>TGA</u>ATAAAGCAGCAGGCCTGTCCTGGCCGGTTGGCTT GACTCTCTCCTGTCAGAATGCAACCTGGCTTTATGCACCTAGATGTCCCCAGCACCCAGTTC TCCATCCCCCACATTCCCCTGTCTGTCCTTGTGATTTGGCATAAAGAGCTTCTGTTTTCTTT **GAAAAAAAAAAAAA**

125/310

FIGURE 122

MAVYVGMLRLGRLCAGSSGVLGARAALSRSWQEARLQGVRFLSSREVDRMVSTPIGGLSYVQ
GCTKKHLNSKTVGQCLETTAQRVPEREALVVLHEDVRLTFAQLKEEVDKAASGLLSIGLCKG
DRLGMWGPNSYAWVLMQLATAQAGIILVSVNPAYQAMELEYVLKKVGCKALVFPKQFKTQQY
YNVLKQICPEVENAQPGALKSQRLPDLTTVISVDAPLPGTLLLDEVVAAGSTRQHLDQLQYN
QQFLSCHDPINIQFTSGTTGSPKGATLSHYNIVNNSNILGERLKLHEKTPEQLRMILPNPLY
HCLGSVAGTMMCLMYGATLILASPIFNGKKALEAISRERGTFLYGTPTMFVDILNQPDFSSY
DISTMCGGVIAGSPAPPELIRAIINKINMKDLVVAYGTTENSPVTFAHFPEDTVEQKAESVG
RIMPHTEARIMNMEAGTLAKLNTPGELCIRGYCVMLGYWGEPQKTEEAVDQDKWYWTGDVAT
MNEQGFCKIVGRSKDMIIRGGENIYPAELEDFFHTHPKVQEVQVVGVKDDRMGEEICACIRL
KDGEETTVEEIKAFCKGKISHFKIPKYIVFVTNYPLTISGKIQKFKLREQMERHLNL

WO 99/63088

127/310

FIGURE 124

GAGCAGGACGGAGCC<u>ATG</u>GACCCCGCCAGGAAAGCAGGTGCCCAGGCCATGATCTGGACTGC AGGCTGGCTGCTGCTGCTTCGCGGAGGAGCGCAGGCCCTGGAGTGCTACAGCTGCG TGCAGAAAGCAGATGACGGATGCTCCCCGAACAAGATGAAGACAGTGAAGTGCGCGCCGGGC GTGGACGTCTGCACCGAGGCCGTGGGGGCGGTGGAGACCATCCACGGACAATTCTCGCTGGC AGTGCGGGGTTGCGGTTCGGGACTCCCCGGCAAGAATGACCGCGGCCTGGATCTTCACGGGC TTCTGGCGTTCATCCAGCTGCAGCAATGCGCTCAGGATCGCTGCAACGCCAAGCTCAACCTC ACCTCGCGGGCGCTCGACCCGGCAGGTAATGAGAGTGCATACCCGCCCAACGGCGTGGAGTG CTACAGCTGTGTGGGCCTGAGCCGGGAGGCGTGCCAGGGTACATCGCCGCCGGTCGTGAGCT GCTACAACGCCAGCGATCATGTCTACAAGGGCTGCTTCGACGGCAACGTCACCTTGACGGCA GCTAATGTGACTGTGCCTTGCCTGTCCGGGGCTGTGTCCAGGATGAATTCTGCACTCGGGA TGGAGTAACAGGCCCAGGGTTCACGCTCAGTGGCTCCTGTTGCCAGGGGTCCCGCTGTAACT CTGACCTCCGCAACAAGACCTACTTCTCCCCTCGAATCCCACCCCTTGTCCGGCTGCCCCCT CCAGAGCCCACGACTGTGGCCTCAACCACATCTGTCACCACTTCTACCTCGGCCCCAGTGAG ACCCACATCCACCACCAAACCCATGCCAGCGCCAACCAGTCAGACTCCGAGACAGGGAGTAG AACACGAGGCCTCCCGGGATGAGGAGCCCAGGTTGACTGGAGGCGCCGCTGGCCACCAGGAC CGCAGCAATTCAGGGCAGTATCCTGCAAAAGGGGGGCCCCAGCAGCCCCCATAATAAAGGCTG TGTGGCTCCCACAGCTGGATTGGCAGCCCTTCTGTTGGCCGTGGCTGCTGGTGTCCTACTG<u>T</u> GAGCTTCTCCACCTGGAAATTTCCCTCTCACCTACTTCTCTGGCCCTGGGTACCCCTCTTCT CATCACTTCCTGTTCCCACCACTGGACTGGGCTGGCCCAGCCCCTGTTTTTCCAACATTCCC CAGTATCCCCAGCTTCTGCTGCGCTGGTTTGCGGCTTTGGGAAATAAAATACCGTTGTATAT ATTCTGCCAGGGGTGTTCTAGCTTTTTGAGGACAGCTCCTGTATCCTTCTCATCCTTGTCTC TCCGCTTGTCCTCTTGTGATGTTAGGACAGAGTGAGAGAGTCAGCTGTCACGGGGAAGGTG GGTGGGTGGGACAATGGCTCCCCACTCTAAGCACTGCCTCCCCTACTCCCCGCATCTTTGGG GAATCGGTTCCCCATATGTCTTCCTTACTAGACTGTGAGCTCCTCGAGGGGGGGCCCGGTAC CCAATTCGCCCTATAGTGAGTCGTA

MDPARKAGAQAMIWTAGWLLLLLRGGAQALECYSCVQKADDGCSPNKMKTVKCAPGVDVCT
EAVGAVETIHGQFSLAVRGCGSGLPGKNDRGLDLHGLLAFIQLQQCAQDRCNAKLNLTSRAL
DPAGNESAYPPNGVECYSCVGLSREACQGTSPPVVSCYNASDHVYKGCFDGNVTLTAANVTV
SLPVRGCVQDEFCTRDGVTGPGFTLSGSCCQGSRCNSDLRNKTYFSPRIPPLVRLPPPEPTT
VASTTSVTTSTSAPVRPTSTTKPMPAPTSQTPRQGVEHEASRDEEPRLTGGAAGHQDRSNSG
QYPAKGGPQQPHNKGCVAPTAGLAALLLAVAAGVLL

FIGURE 126

CGGGACTCGGCGGGTCCTCCTGGGAGTCTCGGAGGGGACCGGCTGTGCAGACGCC<u>ATG</u>GAGT TGGTGCTGGTCTTCCTCTGCAGCCTGCTGGCCCCCATGGTCCTGGCCAGTGCAGCTGAAAAG GAGAAGGAAATGGACCCTTTTCATTATGATTACCAGACCCTGAGGATTGGGGGACTGGTGTT CGCTGTGGTCCTCTTCTCGGTTGGGATCCTCCTTATCCTAAGTCGCAGGTGCAAGTGCAGTT TCAATCAGAAGCCCCGGGCCCCAGGAGATGAGGAAGCCCAGGTGGAGAACCTCATCACCGCC AATGCAACAGAGCCCCAGAAGCAGAGAACTGAAGTGCAGCCATCAGGTGGAAGCCTCTGGAA CCTGAGGCGGCTGCTTGAACCTTTGGATGCAAATGTCGATGCT<u>TAA</u>GAAAACCGGCCACTTC AGCAACAGCCCTTTCCCCAGGAGAAGCCAAGAACTTGTGTGTCCCCCACCCTATCCCCTCTA ACACCATTCCTCCACCTGATGATGCAACTAACACTTGCCTCCCCACTGCAGCCTGCGGTCCT CCCAGGCAGGGGCTGAGCCACATGGCCATCTGCTCCTCCCTGCCCCCGTGGCCCTCCATCAC CTTCTGCTCCTAGGAGGCTGCTTGTTGCCCGAGACCAGCCCCCTCCCCTGATTTAGGGATGC GTAGGGTAAGAGCACGGGCAGTGGTCTTCAGTCGTCTTGGGACCTGGGAAGGTTTGCAGCAC TTTGTCATCATCTTCATGGACTCCTTTCACTCCTTTAACAAAAACCTTGCTTCCTTATCCC ACCTGATCCCAGTCTGAAGGTCTCTTAGCAACTGGAGATACAAAGCAAGGAGCTGGTGAGCC CAGCGTTGACGTCAGGCAGGCTATGCCCTTCCGTGGTTAATTTCTTCCCAGGGGCTTCCACG AGGAGTCCCCATCTGCCCCGCCCCTTCACAGAGCGCCCGGGGATTCCAGGCCCAGGGCTTCT ACTCTGCCCCTGGGGAATGTGTCCCCTGCATATCTTCTCAGCAATAACTCCATGGGCTCTGG GACCCTACCCCTTCCAACCTTCCCTGCTTCTGAGACTTCAATCTACAGCCCAGCTCATCCAG GTTGGGGCCAGCACCGGGATGGATGGAGGGGGAGAGCAGAGGCCTTTGCTTCTCTCCCTACG TCCCCTTAGATGGGCAGCAGAGGCAACTCCCGCATCCTTTGCTCTGCCTGTCGGTGGTCAGA GCGGTGAGCGAGGTGGGTTGGAGACTCAGCAGGCTCCGTGCAGCCCTTGGGAACAGTGAGAG GTTGAAGGTCATAACGAGAGTGGGAACTCAACCCAGATCCCGCCCCTCCTGTCCTCTGTGTT CCCGCGGAAACCAACCAAACCGTGCGCTGTGACCCATTGCTGTTCTCTGTATCGTGATCTAT CCTCAACAACAACAGAAAAAAGGAATAAAATATCCTTTGTTTCCT

MELVLVFLCSLLAPMVLASAAEKEKEMDPFHYDYQTLRIGGLVFAVVLFSVGILLILSRRCK CSFNQKPRAPGDEEAQVENLITANATEPQKQRTEVQPSGGSLWNLRRLLEPLDANVDA

_131/310 FIGURE 128

139/>10 FIGURE 129

 ${\tt MKIPVLPAVVLLSLLVLHSAQGATLGGPEEESTIENYASRPEAFNTPFLNIDKLRSAFKADE}$ ${\tt FLNWHALFESIKRKLPFLNWDAFPKLKGLRSATPDAQ}$

133/510 FIGURE 130

131 FIGURE 131

MGVEIAFASVILTCLSLLAAGVSQVVLLQPVPTQETGPKAMGDLSCGFAGHS

____/35/310 FIGURE 132

GGGGAATCTGCAGTAGGTCTGCCGGCG<u>ATG</u>GAGTGGTGGGCTAGCTCGCCGCTTCGGCTCTG GCTGCTGTTGTTCCTCCTGCCCTCAGCGCAGGGCCCCCAGAAGGAGTCAGGTTCAAAATGGA AAGTATTTATTGACCAAATTAACAGGTCTTTGGAGAATTACGAACCATGTTCAAGTCAAAAC TGCAGCTGCTACCATGGTGTCATAGAAGAGGATCTAACTCCTTTCCGAGGAGGCATCTCCAG GAAGATGATGGCAGAGGTAGTCAGACGGAAGCTAGGGACCCACTATCAGATCACTAAGAACA GACTGTACCGGGAAAATGACTGCATGTTCCCCTCAAGGTGTAGTGGTGTTGAGCACTTTATT TTGGAAGTGATCGGGCGTCTCCCTGACATGGAGATGGTGATCAATGTACGAGATTATCCTCA GGTTCCTAAATGGATGGAGCCTGCCATCCCAGTCTTCTCCTTCAGTAAGACATCAGAGTACC ATGATATCATGTATCCTGCTTGGACATTTTGGGAAGGGGGACCTGCTGTTTGGCCAATTTAT CCTACAGGTCTTGGACGGTGGGACCTCTTCAGAGAAGATCTGGTAAGGTCAGCACAGTG GCCATGGAAAAAGAAAAACTCTACAGCATATTTCCGAGGATCAAGGACAAGTCCAGAACGAG ATCCTCTCATTCTTCTGTCTCGGAAAAACCCAAAACTTGTTGATGCAGAATACACCAAAAAC CAGGCCTGGAAATCTATGAAAGATACCTTAGGAAAGCCAGCTGCTAAGGATGTCCATCTTGT GGATCACTGCAAATACAAGTATCTGTTTAATTTTCGAGGCGTAGCTGCAAGTTTCCGGTTTA AACACCTCTTCCTGTGTGGCTCACTTGTTTTCCATGTTGGTGATGAGTGGCTAGAATTCTTC TATCCACAGCTGAAGCCATGGGTTCACTATATCCCAGTCAAAACAGATCTCTCCAATGTCCA AGAGCTGTTACAATTTGTAAAAGCAAATGATGATGTAGCTCAAGAGATTGCTGAAAGGGGAA GCCAGTTTATTAGGAACCATTTGCAGATGGATGACATCACCTGTTACTGGGAGAACCTCTTG AGTGAATACTCTAAATTCCTGTCTTATAATGTAACGAGAAGGAAAGGTTATGATCAAATTAT TCCCAAAATGTTGAAAACTGAACTA<u>TAG</u>TAGTCATCATAGGACCATAGTCCTCTTTGTGGCA ACAGATCTCAGATATCCTACGGTGAGAAGCTTACCATAAGCTTGGCTCCTATACCTTGAATA TCTGCTATCAAGCCAAATACCTGGTTTTCCTTATCATGCTGCACCCAGAGCAACTCTTGAGA AAGATTTAAAATGTGTCTAATACACTGATATGAAGCAGTTCAACTTTTTGGATGAATAAGGA CCAGAAATCGTGAGATGTGGATTTTGAACCCAACTCTACCTTTCATTTTCTTAAGACCAATC ACAGCTTGTGCCTCAGATCATCCACCTGTGTGAGTCCATCACTGTGAAATTGACTGTGTCCA TGTGATGATGCCCTTTGTCCCATTATTTGGAGCAGAAAATTCGTCATTTGGAAGTAGTACAA CTCATTGCTGGAATTGTGAAATTATTCAAGGCGTGATCTCTGTCACTTTATTTTAATGTAGG AAACCCTATGGGGTTTATGAAAAATACTTGGGGATCATTCTCTGAATGGTCTAAGGAAGCGG TAGCCATGCCATGCAATGATGTAGGAGTTCTCTTTTGTAAAACCATAAACTCTGTTACTCAG GAGGTTTCTATAATGCCACATAGAAAGAGGCCAATTGCATGAGTAATTATTGCAATTGGATT TCAGGTTCCCTTTTTGTGCCCTTCATGCCCTACTTCTTAATGCCTCTCTAAAGCCAAA

136/310 FIGURE 133

MEWWASSPLRLWLLLFLLPSAQGRQKESGSKWKVFIDQINRSLENYEPCSSQNCSCYHGVIE
EDLTPFRGGISRKMMAEVVRRKLGTHYQITKNRLYRENDCMFPSRCSGVEHFILEVIGRLPD
MEMVINVRDYPQVPKWMEPAIPVFSFSKTSEYHDIMYPAWTFWEGGPAVWPIYPTGLGRWDL
FREDLVRSAAQWPWKKKNSTAYFRGSRTSPERDPLILLSRKNPKLVDAEYTKNQAWKSMKDT
LGKPAAKDVHLVDHCKYKYLFNFRGVAASFRFKHLFLCGSLVFHVGDEWLEFFYPQLKPWVH
YIPVKTDLSNVQELLQFVKANDDVAQEIAERGSQFIRNHLQMDDITCYWENLLSEYSKFLSY
NVTRRKGYDQIIPKMLKTEL

-137/310 FIGURE 134

CACCCTCCATTTCTCGCCATGCCCCTGCACTGCTCCTGATCCCTGCTGCCCTCGCCTCTT TCATCCTGGCCTTTGGCACCGGAGTGGAGTTCGTGCGCTTTACCTCCCTTCGGCCACTTCTT CCGCAGCATCCTTGCCCCCCTGGCATGGGATCTGGGGCTCCTGCTTCTATTTGTTGGGCAGC ACAGCCTCATGGCAGCTGAAAGAGTGAAGGCATGGACATCCCGGTACTTTGGGGTCCTTCAG AGGTCACTGTATGTGGCCTGCACTGCCCTGGCCTTGCAGCTGGTGATGCGGTACTGGGAGCC CATACCCAAAGGCCCTGTGTTGTGGGAGGCTCGGGCTGAGCCATGGGCCACCTGGGTGCCGC TCCTCTGCTTTGTGCTCCATGTCATCTCCTGGCTCCTCATCTTTAGCATCCTTCTCGTCTTT GACTATGCTGAGCTCATGGGCCTCAAACAGGTATACTACCATGTGCTGGGGCTGGGCGAGCC TCTGGCCCTGAAGTCTCCCCGGGCTCTCAGACTCTTCTCCCACCTGCGCCACCCAGTGTGTG TGGAGCTGCTGACAGTGCTGTGGGTGCCTACCCTGGGCACGGACCGTCTCCTCCTTGCT TTCCTCCTTACCCTCTACCTGGGCCTGGCTCACGGGCTTGATCAGCAAGACCTCCGCTACCT CCGGGCCCAGCTACAAAGAAAACTCCACCTGCTCTCTCGGCCCCAGGATGGGGAGGCAGAGT GAGGAGCTCACTCTGGTTACAAGCCCTGTTCTTCCTCTCCCACTGAATTCTAAATCCTTAAC ATCCAGGCCCTGGCTGCTTCATGCCAGAGGCCCAAATCCATGGACTGAAGGAGATGCCCCTT CTACTACTTGAGACTTTATTCTCTGGGTCCAGCTCCATACCCTAAATTCTGAGTTTCAGCCA CTGAACTCCAAGGTCCACTTCTCACCAGCAAGGAAGAGTGGGGTATGGAAGTCATCTGTCCC TTCACTGTTTAGAGCATGACACTCTCCCCCTCAACAGCCTCCTGAGAAGGAAAGGATCTGCC CTGACCACTCCCCTGGCACTGTTACTTGCCTCTGCGCCTCAGGGGTCCCCTTCTGCACCGCT GGCTTCCACTCCAAGAAGGTGGACCAGGGTCTGCAAGTTCAACGGTCATAGCTGTCCCTCCA GGCCCAACCTTGCCTCACCACTCCCGGCCCTAGTCTCTGCACCTCCTTAGGCCCTGCCTCT GGGCTCAGACCCAACCTAGTCAAGGGGATTCTCCTGCTCTTAACTCGATGACTTGGGGCTC

_138/310 FIGURE 135

MAPALLLIPAALASFILAFGTGVEFVRFTSLRPLLGGIPESGGPDARQGWLAALQDRSILAP LAWDLGLLLLFVGQHSLMAAERVKAWTSRYFGVLQRSLYVACTALALQLVMRYWEPIPKGPV LWEARAEPWATWVPLLCFVLHVISWLLIFSILLVFDYAELMGLKQVYYHVLGLGEPLALKSP RALRLFSHLRHPVCVELLTVLWVVPTLGTDRLLLAFLLTLYLGLAHGLDQQDLRYLRAQLQR KLHLLSRPQDGEAE

CCGAGCACAGGAGATTGCCTGCGTTTAGGAGGTGGCTGCGTTGTGGGAAAAGCTATCAAGGA AGAAATTGCCAAACCATGTCTTTTTTCTGTTTTCAGAGTAGTTCACAACAGATCTGAGTGT TTTAATTAAGCATGGAATACAGAAAACAACAAAAAACTTAAGCTTTAATTTCATCTGGAATT TCACGTGGTGCTCTCCGACTACTCACCCCGAGTGTAAAGAACCTTCGGCTCGCGTGCTTCTG AGCTGCTGTGGATGGCCTCGGCTCTCTGGACTGTCCTTCCGAGTAGGATGTCACTGAGATCC CTCAAATGGAGCCTCCTGCTGCTGTCACTCCTGAGTTTCTTTGTGATGTGGTACCTCAGCCT TCCCCACTACAATGTGATAGAACGCGTGAACTGGATGTACTTCTATGAGTATGAGCCGATTT ACAGACAAGACTTTCACTTCACACTTCGAGAGCATTCAAACTGCTCTCATCAAAATCCATTT TTGGGGTGAAAAAAGTCTTGGTGGGGATATGAGGTTCTTACATTTTTCTTATTAGGCCAAG AGGCTGAAAAGGAAGACAAAATGTTGGCATTGTCCTTAGAGGATGAACACCTTCTTTATGGT GACATAATCCGACAAGATTTTTTAGACACATATAATAACCTGACCTTGAAAACCATTATGGC TTTTCATCAATACTGGCAATTTAGTGAAGTATCTTTTAAACCTAAACCACTCAGAGAAGTTT TTCACAGGTTATCCTCTAATTGATAATTATTCCTATAGAGGATTTTACCAAAAAACCCATAT TTCTTACCAGGAGTATCCTTTCAAGGTGTTCCCTCCATACTGCAGTGGGTTGGGTTATATAA TGTCCAGAGATTTGGTGCCAAGGATCTATGAAATGATGGGTCACGTAAAACCCATCAAGTTT GAAGATGTTTATGTCGGGATCTGTTTGAATTTATTAAAAGTGAACATTCATATTCCAGAAGA CAGCCCATGGCTTTTCTTCCAAGGAGATCATCACTTTTTGGCAGGTCATGCTAAGGAACACC ACATGCCATTAT<u>TAA</u>CTTCACATTCTACAAAAAGCCTAGAAGGACAGGATACCTTGTGGAAA GTGTTAAATAAAGTAGGTACTGTGGAAAATTCATGGGGAGGTCAGTGTGCTGGCTTACACTG AACTGAAACTCATGAAAAACCCAGACTGGAGGACTGGAGGGTTACACTTGTGATTTATTAGTC AGGCCCTTCAAAGATGATATGTGGAGGAATTAAATATAAAGGAATTGGAGGTTTTTGCTAAA GAAATTAATAGGACCAAACAATTTGGACATGTCATTCTGTAGACTAGAATTTCTTAAAAGGG AACAATGTAGTCACTTGAAGGTTTTGTGTATATCTTATGTGGATTACCAATTTAAAAATATA TGTAGTTCTGTGTCAAAAAACTTCTTCACTGAAGTTATACTGAACAAAATTTTACCTGTTTT TGGTCATTTATAAAGTACTTCAAGATGTTGCAGTATTTCACAGTTATTATTATTAAAATTA CTTCAACTTTGTGTTTTTAAATGTTTTGACGATTTCAATACAAGATAAAAAGGATAGTGAAT CATTCTTTACATGCAAACATTTTCCAGTTACTTAACTGATCAGTTTATTATTGATACATCAC TCCATTAATGTAAAGTCATAGGTCATTATTGCATATCAGTAATCTCTTGGACTTTGTTAAAT ATTTTACTGTGGTAATATAGAGAAGAATTAAAGCAAGAAAATCTGAAAA

_ио/310 FIGURE 137

MASALWTVLPSRMSLRSLKWSLLLLSLLSFFVMWYLSLPHYNVIERVNWMYFYEYEPIYRQD FHFTLREHSNCSHQNPFLVILVTSHPSDVKARQAIRVTWGEKKSWWGYEVLTFFLLGQEAEK EDKMLALSLEDEHLLYGDIIRQDFLDTYNNLTLKTIMAFRWVTEFCPNAKYVMKTDTDVFIN TGNLVKYLLNLNHSEKFFTGYPLIDNYSYRGFYQKTHISYQEYPFKVFPPYCSGLGYIMSRD LVPRIYEMMGHVKPIKFEDVYVGICLNLLKVNIHIPEDTNLFFLYRIHLDVCQLRRVIAAHG FSSKEIITFWQVMLRNTTCHY

_____/310 FIGURE 138

MKFTIVFAGLLGVFLAPALANYNINVNDDNNNAGSGQQSVSVNNEHNVANVDNNNGWDSWNS IWDYGNGFAATRLFQKKTCIVHKMNKEVMPSIQSLDALVKEKKLQGKGPGGPPPKGLMYSVN PNKVDDLSKFGKNIANMCRGIPTYMAEEMQEASLFFYSGTCYTTSVLWIVDISFCGDTVEN

CATTTCTGAAACTAATCGTGTCAGAATTGACTTTGAAAAGCATTGCTTTTTACAGAAGTATA TTAACTTTTTAGGAGTAATTTCTAGTTTGGATTGTAATATGAAATAATTTAAAAGGGCTTCG CTCATATATAGGAAAATCGCATATGGTCCTAGTATTAAATTCTTATTGCTTACTGATTTTTT TTGTTCGATTTCAACCAGAGACTATAGCATGTGCTTGCATCTACCTTGCAGCTAGAGCACTT CAGATTCCGTTGCCAACTCGTCCCCATTGGTTTCTTCTTTTTGGTACTACAGAAGAGGAAAT CCAGGAAATCTGCATAGAAACACTTAGGCTTTATACCAGAAAAAAGCCAAACTATGAATTAC TGGAAAAAGAAGTAGAAAAAAAGAAAGTAGCCTTACAAGAAGCCAAATTAAAAGCAAAGGGA TTGAATCCGGATGGAACTCCAGCCCTTTCAACCCTGGGTGGATTTTCTCCAGCCTCCAAGCC ATCATCACCAAGAGAAGTAAAAGCTGAAGAGAAATCACCAATCTCCATTAATGTGAAGACAG TCAAAAAAGAACCTGAGGATAGACAACAGGCTTCCAAAAGCCCCTTACAATGGTGTAAGAAAA TTCTAGATCACATACTCCAAGAAGACACTATAATAATAGGCGGAGTCGATCTGGAACATACA GCTCGAGATCAAGAAGCAGGTCCCGCAGTCACAGTGAAAGCCCTCGAAGACATCATAATCAT GGTTCTCCTCACCTTAAGGCCAAGCATACCAGAGATGATTTAAAAAGTTCAAACAGACATGG TCATAAAAGGAAAAAATCTCGTTCTCGATCTCAGAGCAAGTCTCGGGATCACTCAGATGCAG CCAAGAAACACAGGCATGAAAGGGGACATCATAGGGACAGGCGTGAACGATCTCGCTCCTTT $C\underline{TGA}CTTTCTCTTTCGAGCCTGCATCAGTTCTTGGTTTTTGCCTATCTACAGTGTGATGT$ ATGGACTCAATCAAAAACATTAAACGCAAACTGATTAGGATTTGATTTCTTGAAACCCTCTA AAAATGCCCTAGCAGTATCTAATTAAAAACCATGGTCAGGTTCAATTGTACTTTATTATAGT TGTGTATTGTTTATTGCTATAAGAACTGGAGCGTGAATTCTGTAAAAATGTATCTTATTTTT ATACAGATAAAATTGCAGACACTGTTCTATTTAAGTGGTTATTTGTTTAAATGATGGTGAAT ACTTTCTTAACACTGGTTTGTCTGCATGTGTAAAGATTTTTACAAGGAAATAAAATACAAAT CTTGTTTTTCTAAAAAAAAAAAAAAAAAAAAGT

ユ44/210 FIGURE 141

MNDSLRTNVFVRFQPETIACACIYLAARALQIPLPTRPHWFLLFGTTEEEIQEICIETLRLY
TRKKPNYELLEKEVEKRKVALQEAKLKAKGLNPDGTPALSTLGGFSPASKPSSPREVKAEEK
SPISINVKTVKKEPEDRQQASKSPYNGVRKDSKRSRNSRSASRSRSRTRSRSRSHTPRRHYN
NRRSRSGTYSSRSRSRSRSHSESPRRHHNHGSPHLKAKHTRDDLKSSNRHGHKRKKSRSRSQ
SKSRDHSDAAKKHRHERGHHRDRRERSRSFERSHKSKHHGGSRSGHGRHRR

FIGURE 142

_____6/3-10 FIGURE 143

 ${\tt GGCACGAGGCCTCGTGCCAAGCTTGGCACGAGGGTGCACCGCGTTCTCGCACGCGTC} \underline{{\tt ATG}}{\tt GC}$ GGTCCTCGGAGTACAGCTGGTGACCCTGCTCACTGCCACCCTCATGCACAGGCTGGCGC CACACTGCTCCTTCGCGCGCTGGCTGCTCTGTAACGGCAGTTTGTTCCGATACAAGCACCCG TCTGAGGAGGAGCTTCGGGCCCTGGCGGGAAGCCGAGGCCCAGAGGCAGGAAAGAGCGGTG GGCCAATGGCCTTAGTGAGGAGAAGCCACTGTCTGTGCCCCGAGATGCCCCGTTCCAGCTGG AGACCTGCCCCTCACGACCGTGGATGCCCTGGTCCTGCGCTTCTTCCTGGAGTACCAGTGG ${\tt TTTGTGGACTTTGCTGTGTACTCGGGCGGCGTGTACCTCTTCACAGAGGCCTACTACTACAT}$ GCTGGGACCAGCCAAGGAGACTAACATTGCTGTTCTGGTGCCTGCTCACGGTGACCTTCT CCATCAAGATGTTCCTGACAGTGACACGGCTGTACTTCAGCGCCGAGGAGGGGGGGTGAGCGC TCTGTCTGCCTCACCTTTGCCTTCCTCTTCCTGCTGCCATGCTGGTGCAAGTGGTGCG GGAGGAGACCCTCGAGCTGGGCCTGGAGCCTGGTCTGGCCAGCATGACCCAGAACTTAGAGC CACTTCTGAAGAAGCAGGGCTGGGACTGGGCGCTTCCTGTGGCCAAGCTGGCTATCCGCGTG GGACTGGCAGTGGTGGGCTCTGTGCTGGGTGCCTTCCTCACCTTCCCAGGCCTGCGGCTGGC CCAGACCCACCGGGACGCACTGACCATGTCGGAGGACAGACCCATGCTGCAGTTCCTCCTGC ACACCAGCTTCCTGTCTCCCCTGTTCATCCTGTGGCTCTGGACAAAGCCCATTGCACGGGAC TTCCTGCACCAGCCGCCGTTTGGGGAGACGCGTTTCTCCCTGCTGTCCGATTCTGCCTTCGA ACCTGCAGGCCTACCTGTGCCTGGCCAAGGCCCGGGTGGAGCAGCTGCGAAGGGAGGCTGGC CGCATCGAAGCCCGTGAAATCCAGCAGAGGGTGGTCCGAGTCTACTGCTATGTGACCGTGGT GAGCTTGCAGTACCTGACGCCGCTCATCCTCACCCTCAACTGCACACTTCTGCTCAAGACGC TGGGAGGCTATTCCTGGGGCCTGGGCCCAGCTCCTCTACTATCCCCCGACCCATCCTCAGCC AGCGCTGCCCCATCGGCTCTGGGGAGGACGAAGTCCAGCAGACTGCAGCGCGGATTGCCGG GGCCCTGGGTGGCCTGCTTACTCCCCCTCTTCCTCCGTGGCGTCCTGGCCTACCTCATCTGGT GGACGGCTGCCAGCTGCTCGCCAGCCTTTTCGGCCTCTACTTCCACCAGCACTTGGCA ${\tt GGCTCC\underline{TAG}CTGCCTGCAGACCCTCCTGGGGCCCTGAGGTCTGTTCCTGGGGCAGCGGGACA}$ CTAGCCTGCCCCTCTGTTTGCGCCCCCGTGTCCCCAGCTGCAAGGTGGGGCCGGACTCCCC GGCGTTCCCTTCACCACAGTGCCTGACCCGCGGCCCCCTTGGACGCCGAGTTTCTGCCTCA GAACTGTCTCTCCTGGGCCCAGCAGCATGAGGGTCCCGAGGCCATTGTCTCCGAAGCGTATG TGCCAGGTTTGAGTGGCGAGGGTGATGCTGGCTGCTCTTCTGAACAAATAAAGGAGCATGCC GATTTTTAA

MAVLGVQLVVTLLTATLMHRLAPHCSFARWLLCNGSLFRYKHPSEEELRALAGKPRPRGRKE RWANGLSEEKPLSVPRDAPFQLETCPLTTVDALVLRFFLEYQWFVDFAVYSGGVYLFTEAYY YMLGPAKETNIAVFWCLLTVTFSIKMFLTVTRLYFSAEEGGERSVCLTFAFLFLLLAMLVQV VREETLELGLEPGLASMTQNLEPLLKKQGWDWALPVAKLAIRVGLAVVGSVLGAFLTFPGLR LAQTHRDALTMSEDRPMLQFLLHTSFLSPLFILWLWTKPIARDFLHQPPFGETRFSLLSDSA FDSGRLWLLVVLCLLRLAVTRPHLQAYLCLAKARVEQLRREAGRIEAREIQQRVVRVYCYVT VVSLQYLTPLILTLNCTLLLKTLGGYSWGLGPAPLLSPDPSSASAAPIGSGEDEVQQTAARI AGALGGLLTPLFLRGVLAYLIWWTAACQLLASLFGLYFHQHLAGS

FIGURE 145

FIGURE 146

GGTTCCTACATCCTCATCTGAGAATCAGAGAGCATAATCTTCTTACGGGCCCCGTGATTTA TTAACGTGGCTTAATCTGAAGGTTCTCAGTCAAATTCTTTGTGATCTACTGATTGTGGGGGC ATGGCAAGGTTTGCTTAAAGGAGCTTGGCTGGTTTGGGCCCTTGTAGCTGACAGAAGGTGGC CAGGGAGAATGCAGCACACTGCTCGGAGA<u>ATG</u>AAGGCGCTTCTGTTGCTGGTCTTGCCTTGG CTCAGTCCTGCTAACTACATTGACAATGTGGGCAACCTGCACTTCCTGTATTCAGAACTCTG TAAAGGTGCCTCCCACTACGGCCTGACCAAAGATAGGAAGAGGCGCTCACAAGATGGCTGTC CAGACGGCTGTGCGAGCCTCACAGCCACGGCTCCCTCCCCAGAGGTTTCTGCAGCTGCCACC ATCTCCTTAATGACAGACGAGCCTGGCCTAGACAACCCTGCCTACGTGTCCTCGGCAGAGGA CGGGCAGCCAGCAATCAGCCCAGTGGACTCTGGCCGGAGCAACCGAACTAGGGCACGGCCCT CGAAGGACAAAGAGCGGGAGTGCAGTTGCCAACCATGCCGACCAGGGCAGGGAAAATTCTGA AAACACCACTGCCCCTGAAGTCTTTCCAAGGTTGTACCACCTGATTCCAGATGGTGAAATTA CCAGCATCAAGATCAATCGAGTAGATCCCAGTGAAAGCCTCTCTATTAGGCTGGTGGGAGGT AGCGAAACCCCACTGGTCCATATCATTATCCAACACATTTATCGTGATGGGGTGATCGCCAG AGACGGCCGGCTACTGCCAGGAGACATCATTCTAAAGGTCAACGGGATGGACATCAGCAATG TCCCTCACAACTACGCTGTGCGTCTCCTGCGGCAGCCCTGCCAGGTGCTGTGGCTGACTGTG ATGCGTGAACAGAAGTTCCGCAGCAGGAACAATGGACAGGCCCCGGATGCCTACAGACCCCG AGATGACAGCTTTCATGTGATTCTCAACAAAAGTAGCCCCGAGGAGCAGCTTGGAATAAAAC TGGTGCGCAAGGTGGATGAGCCTGGGGTTTTCATCTTCAATGTGCTGGATGGCGGTGTGGCA TATCGACATGGTCAGCTTGAGGAGAATGACCGTGTTTAGCCATCAATGGACATGATCTTCG ATATGGCAGCCCAGAAAGTGCGGCTCATCTGATTCAGGCCAGTGAAAGACGTGTTCACCTCG TCGTGTCCCGCCAGGTTCGGCAGCGGAGCCCTGACATCTTTCAGGAAGCCGGCTGGAACAGC AATGGCAGCTGGTCCCCAGGGCCAGGGGAGAGAGCAACACTCCCAAGCCCCTCCATCCTAC AATTACTTGTCATGAGAAGGTGGTAAATATCCAAAAAGACCCCGGTGAATCTCTCGGCATGA CCCGGAGGAGTCATAAGCAGAGATGGAAGAATAAAAACAGGTGACATTTTGTTGAATGTGGA TGGGGTCGAACTGACAGAGGTCAGCCGGAGTGAGGCAGTGGCATTATTGAAAAGAACATCAT CCTCGATAGTACTCAAAGCTTTGGAAGTCAAAGAGTATGAGCCCCAGGAAGACTGCAGCAGC CATGTGGCTGGAATTACCACGGTGCTTGTATAACTGTAAAGATATTGTATTACGAAGAAACA TTTTTCATCAAATCCATTGTTGAAGGAACACCAGCATACAATGATGGAAGAATTAGATGTGG GACTGCTGAAAGAACTTAAAGGAAGAATTACTCTAACTATTGTTTCTTGGCCTGGCACTTTT TTA<u>TAG</u>AATCAATGATGGGTCAGAGGAAAACAGAAAAATCACAAATAGGCTAAGAAGTTGAA AAAAGTATGATCATCTAATGAAAGCCAGTTACACCTCAGAAAATATGATTCCAAAAAAATTA AAACTACTAGTTTTTTTCAGTGTGGAGGATTTCTCATTACTCTACAACATTGTTTATATTT CAAGCTGATTTAAAATTTGGTATATGCTGAAGTCTGCCAAGGGTACATTATGGCCA TTTTTAATTTACAGCTAAAATATTTTTTAAAATGCATTGCTGAGAAACGTTGCTTTCATCAA ACAAGAATAAATATTTTTCAGAAGTTAAA

150/310 FIGURE 147

MKALLLLVLPWLSPANYIDNVGNLHFLYSELCKGASHYGLTKDRKRRSQDGCPDGCASLTAT
APSPEVSAAATISLMTDEPGLDNPAYVSSAEDGQPAISPVDSGRSNRTRARPFERSTIRSRS
FKKINRALSVLRRTKSGSAVANHADQGRENSENTTAPEVFPRLYHLIPDGEITSIKINRVDP
SESLSIRLVGGSETPLVHIIIQHIYRDGVIARDGRLLPGDIILKVNGMDISNVPHNYAVRLL
RQPCQVLWLTVMREQKFRSRNNGQAPDAYRPRDDSFHVILNKSSPEEQLGIKLVRKVDEPGV
FIFNVLDGGVAYRHGQLEENDRVLAINGHDLRYGSPESAAHLIQASERRVHLVVSRQVRQRS
PDIFQEAGWNSNGSWSPGPGERSNTPKPLHPTITCHEKVVNIQKDPGESLGMTVAGGASHRE
WDLPIYVISVEPGGVISRDGRIKTGDILLNVDGVELTEVSRSEAVALLKRTSSSIVLKALEV
KEYEPQEDCSSPAALDSNHNMAPPSDWSPSWVMWLELPRCLYNCKDIVLRRNTAGSLGFCIV
GGYEEYNGNKPFFIKSIVEGTPAYNDGRIRCGDILLAVNGRSTSGMIHACLARLLKELKGRI

FIGURE 148

FIGURE 149

MKILVAFLVVLTIFGIQSHGYEVFNIISPSNNGGNVQETVTIDNEKNTAIVNIHAGSCSSTT IFDYKHGYIASRVLSRRACFILKMDHQNIPPLNNLQWYIYEKQALDNMFSNKYTWVKYNPLE SLIKDVDWFLLGSPIEKLCKHIPLYKGEVVENTHNVGAGGCAKAGLLGILGISICADIHV

FIGURE 150

GGAGGAAGAATTACCCCTGTGGTCTCCATTGCCTACAAAGTCCTGGAAGTTTTCCCCAAAG GCCGCTGGGTGCTCATAACCTGCTGTGCACCCCAGCCACCACCGCCCATCACCTATTCCCTC TGTGGAACCAAGAACATCAAGGTGGCCAAGAAGGTGGTGAAGACCCACGAGCCGGCCTCCTT CAACCTCAACGTCACACTCAAGTCCAGTCCAGACCTGCTCACCTACTTCTGCCGGGCGTCCT CCACCTCAGGTGCCCATGTGGACAGTGCCAGGCTACAGATGCACTGGGAGCTGTGGTCCAAG CCAGTGTCTGAGCTGCGGGCCAACTTCACTCTGCAGGACAGAGGGGCAGGCCCCAGGGTGGA GATGATCTGCCAGGCGTCCTCGGGCAGCCCACCTATCACCAACAGCCTGATCGGGAAGGATG AGCCAGACATCGGACTGGTTCTGGTGCCAGGCTGCAAACAACGCCCAATGTCCAGCACAGCGC CCTCACAGTGGTGCCCCCAGGTGGTGACCAGAAGATGGAGGACTGGCAGGGTCCCCTGGAGA GCCCCATCCTTGCCTTGCCGCTCTACAGGAGCACCCGCCGTCTGAGTGAAGAGGAGTTTGGG GGGTTCAGGATAGGGAATGGGGAGGTCAGAGGACGCAAAGCAGCAGCCATG<u>TAG</u>AATGAACC GTCCAGAGAGCCAAGCACGGCAGAGGACTGCAGGCCATCAGCGTGCACTGTTCGTATTTGGA

FIGURE 151

MGLPGLFCLAVLAASSFSKAREEEITPVVSIAYKVLEVFPKGRWVLITCCAPQPPPPITYSL CGTKNIKVAKKVVKTHEPASFNLNVTLKSSPDLLTYFCRASSTSGAHVDSARLQMHWELWSK PVSELRANFTLQDRGAGPRVEMICQASSGSPPITNSLIGKDGQVHLQQRPCHRQPANFSFLP SQTSDWFWCQAANNANVQHSALTVVPPGGDQKMEDWQGPLESPILALPLYRSTRRLSEEEFG GFRIGNGEVRGRKAAAM

155/310 FIGURE 152

GGTCCTTAATGGCAGCAGCCGCCGCTACCAAGATCCTTCTGTGCCTCCCGCTTCTGCTCCTG CTGTCCGGCTGGTCCCGGGCTGGGCGAGCCGACCCTCACTCTTTTGCTATGACATCACCGT CATCCCTAAGTTCAGACCTGGACCACGGTGGTGTGCGGTTCAAGGCCAGGTGGATGAAAAGA CTTTTCTTCACTATGACTGTGGCAACAAGACAGTCACCTGTCAGTCCCCTGGGGAAGAAA CTAAATGTCACAACGGCCTGGAAAGCACAGAACCCAGTACTGAGAGAGGTGGTGGACATACT TACAGAGCAACTGCGTGACATTCAGCTGGAGAATTACACCCCAAGGAACCCCTCACCCTGC AGGCAAGGATGTCTTGTGAGCAGAAAGCTGAAGGACACAGCAGTGGATCTTGGCAGTTCAGT TGGAGCCAGAAGATGAAAGAAAAGTGGGAGAATGACAAGGTTGTGGCCATGTCCTTCCATT **ACTTCTCAATGGGAGACTGTATAGGATGGCTTGAGGACTTCTTGATGGGCATGGACAGCACC** CTGGAGCCAAGTGCAGGAGCACCACTCGCCATGTCCTCAGGCACAACCCCAACTCAGGGCCAC AGCCACCACCTCATCCTTTGCTGCCTCCTCATCATCCTCCCCTGCTTCATCCTCCCTGGCA TCTGAGGAGAGTCCTTTAGAGTGACAGGTTAAAGCTGATACCAAAAGGCTCCTGTGAGCACG GTCTTGATCAAACTCGCCCTTCTGTCTGGCCAGGCTGCCCACGACCTACGGTGTATGTCCAGT **GGCTCCAGCAGATCATGATGACATCATGGACCCAATAGCTCATTCACTGCCTTGATTCCTT** TTGCCAACAATTTTACCAGCAGTTATACCTAACATATTATGCAATTTTCTCTTGGTGCTACC GTCAGTAAAATAATCACGTTAGACTTCAGACCTCTGGGGATTCTTTCCGTGTCCTGAAAGAG **AATTTTTAAATTATTTAATAAGAAAAATTTATTATTAATGATTGTTTCCTTTAGTAATTTAT**

156/310 FIGURE 153

MAAAAATKILLCLPLLLLLSGWSRAGRADPHSLCYDITVIPKFRPGPRWCAVQGQVDEKTFL HYDCGNKTVTPVSPLGKKLNVTTAWKAQNPVLREVVDILTEQLRDIQLENYTPKEPLTLQAR MSCEQKAEGHSSGSWQFSFDGQIFLLFDSEKRMWTTVHPGARKMKEKWENDKVVAMSFHYFS MGDCIGWLEDFLMGMDSTLEPSAGAPLAMSSGTTQLRATATTLILCCLLIILPCFILPGI

J5千/310 ・ **FIGURE 154**

158/310 FIGURE 155

MELIPTITSWRVLILVVALTQFWCGFLCRGFHLQNHELWLLIKREFGFYSKSQYRTWQKKLA EDSTWPPINRTDYSGDGKNGFYINGGYESHEQIPKRKLKLGGQPTEQHFWARL

FIGURE 156

GTTCTCCTTTCCGAGCCAAAATCCCAGGCGATGGTGAATTATGAACGTGCCACACCATGAAG CTCTTGTGGCAGGTAACTGTGCACCACCACCCTGGAATGCCATCCTGCTCCCGTTCGTCTA CCTCACGCGCAAGTGTGGATTCTGTGTGCAGCCATCGCTGCTGCCGCCTCAGCCGGGCCCC AGAACTGCCCCTCCGTTTGCTCGTGCAGTAACCAGTTCAGCAAGGTGGTGTGCACGCGCCGG GGCCTCTCCGAGGTCCCGCAGGGTATTCCCTCGAACACCCGGTACCTCAACCTCATGGAGAA CAACATCCAGATGATCCAGGCCGACACCTTCCGCCACCTCCACCACCTGGAGGTCCTGCAGT TGGGCAGGAACTCCATCCGGCAGATTGAGGTGGGGGCCTTCAACGGCCTGGCCAGCCTCAAC ACCTGGAGCTGTTCGACAACTGGCTGACAGTCATCCCTAGCGGGGCCTTTGAATACCTGTC CAAGCTGCGGGAGCTCTGGCTTCGCAACAACCCCATCGAAAGCATCCCCTCTTACGCCTTCA ACCGGGTGCCCTCCCTCATGCGCCTGGACTTGGGGGAGCTCAAGAAGCTGGAGTATATCTCT GAGGGAGCTTTTGAGGGGCTGTTCAACCTCAAGTATCTGAACTTGGGCATGTGCAACATTAA AGACATGCCCAATCTCACCCCCCTGGTGGGGCTGGAGGAGCTGGAGATGTCAGGGAACCACT TCCCTGAGATCAGGCCTGGCTCCTTCCATGGCCTGAGCTCCCTCAAGAAGCTCTGGGTCATG CAACTTGGCCCACAATAACCTCTCTTCTTTGCCCCATGACCTCTTTACCCCGCTGAGGTACC TGGTGGAGTTGCATCTACACCACAACCCTTGGAACTGTGATTGTGACATTCTGTGGCTAGCC TGGTGGCTTCGAGAGTATATACCCACCAATTCCACCTGCTGTGGCCGCTGTCATGCTCCCAT GCACATGCGAGGCCGCTACCTCGTGGAGGTGGACCAGGCCTCCTTCCAGTGCTCTGCCCCCT TCATCATGGACGCACCTCGAGACCTCAACATTTCTGAGGGTCGGATGGCAGAACTTAAGTGT CGGACTCCCCTATGTCCTCCGTGAAGTGGTTGCTGCCCAATGGGACAGTGCTCAGCCACGC CTCCCGCCACCCAAGGATCTCTGTCCTCAACGACGCCACCTTGAACTTTTCCCACGTGCTGC TTTCAGACACTGGGGTGTACACATGCATGGTGACCAATGTTGCAGGCAACTCCAACGCCTCG GCCTACCTCAATGTGAGCACGGCTGAGCTTAACACCTCCAACTACAGCTTCTTCACCACAGT AACAGTGGAGACCACGGAGATCTCGCCTGAGGACACAACGCGAAAGTACAAGCCTGTTCCTA CCACGTCCACTGGTTACCAGCCGGCATATACCACCTCTACCACGGTGCTCATTCAGACTACC CGTGTGCCCAAGCAGGTGGCAGTACCCGCGACAGACACCACTGACAAGATGCAGACCAGCCT GGATGAAGTCATGAAGACCACCAAGATCATCATTGGCTGCTTTGTGGCAGTGACTCTGCTAG CTGCCGCCATGTTGATTGTCTTCTATAAACTTCGTAAGCGGCACCAGCAGCGGAGTACAGTC ACAGCCGCCCGGACTGTTGAGATAATCCAGGTGGACGAAGACATCCCAGCAGCAACATCCGC AGCAGCAACAGCAGCTCCGTCCGGTGTATCAGGTGAGGGGGCAGTAGTGCTGCCCACAATTC ATGACCATATTAACTACAACACCTACAAACCAGCACATGGGGCCCACTGGACAGAAAACAGC CTGGGGAACTCTCTGCACCCCACAGTCACCACTATCTCTGAACCTTATATAATTCAGACCCA TACCAAGGACAAGGTACAGGAAACTCAAATA<u>TGA</u>CTCCCCTCCCCAAAAAACTTATAAAAT **GCAATAGAATGCACAAAGACAGCAACTTTTGTACAGAGTGGGGAGAGACTTTTTCTTGTA** TATGCTTATATATTAAGTCTATGGGCTGGTTAAAAAAAACAGATTATATTAAAATTTAAAGA CAAAAAGTCAAAACA

FIGURE 157

MKLLWQVTVHHHTWNAILLPFVYLTAQVWILCAAIAAAASAGPQNCPSVCSCSNQFSKVVCT
RRGLSEVPQGIPSNTRYLNLMENNIQMIQADTFRHLHHLEVLQLGRNSIRQIEVGAFNGLAS
LNTLELFDNWLTVIPSGAFEYLSKLRELWLRNNPIESIPSYAFNRVPSLMRLDLGELKKLEY
ISEGAFEGLFNLKYLNLGMCNIKDMPNLTPLVGLEELEMSGNHFPEIRPGSFHGLSSLKKLW
VMNSQVSLIERNAFDGLASLVELNLAHNNLSSLPHDLFTPLRYLVELHLHHNPWNCDCDILW
LAWWLREYIPTNSTCCGRCHAPMHMRGRYLVEVDQASFQCSAPFIMDAPRDLNISEGRMAEL
KCRTPPMSSVKWLLPNGTVLSHASRHPRISVLNDGTLNFSHVLLSDTGYYTCMVTNVAGNSN
ASAYLNVSTAELNTSNYSFFTTVTVETTEISPEDTTRKYKPVPTTSTGYQPAYTTSTTVLIQ
TTRVPKQVAVPATDTTDKMQTSLDEVMKTTKIIIGCFVAVTLLAAAMLIVFYKLRKRHQQRS
TVTAARTVEIIQVDEDIPAATSAAATAAPSGVSGEGAVVLPTIHDHINYNTYKPAHGAHWTE
NSLGNSLHPTVTTISEPYIIQTHTKDKVQETQI

FIGURE 158

CGCTCGGGCACCAGCCGCGCAAGG<u>ATG</u>GAGCTGGGTTGCTGGACGCAGTTGGGGCTCACTT TTCTTCAGCTCCTTCTCATCTCGTCCTTGCCAAGAGAGTACACAGTCATTAATGAAGCCTGC CCTGGAGCAGAGTGGAATATCATGTGTCGGGAGTGCTGTGAATATGATCAGATTGAGTGCGT CTGCCCGGAAAGAGGGAAGTCGTGGGTTATACCATCCCTTGCTGCAGGAATGAGGAGAATG AGTGTGACTCCTGCCTGATCCACCCAGGTTGTACCATCTTTGAAAACTGCAAGAGCTGCCGA AATGGCTCATGGGGGGGTACCTTGGATGACTTCTATGTGAAGGGGTTCTACTGTGCAGAGTG CCGAGCAGGCTGGTACGGAGGAGACTGCATGCGATGTGGCCAGGTTCTGCGAGCCCCAAAGG GTCAGATTTTGTTGGAAAGCTATCCCCTAAATGCTCACTGTGAATGGACCATTCATGCTAAA CCTGGGTTTGTCATCCAACTAAGATTTGTCATGTTGAGTCTGGAGTTTGACTACATGTGCCA GTATGACTATGTTGAGGTTCGTGATGGAGACAACCGCGATGGCCAGATCATCAAGCGTGTCT GTGGCAACGAGCGGCCAGCTCCTATCCAGAGCATAGGATCCTCACTCCACGTCCTCTTCCAC TCCGATGGCTCCAAGAATTTTGACGGTTTCCATGCCATTTATGAGGAGATCACAGCATGCTC CTCATCCCCTTGTTTCCATGACGGCACGTGCGTCCTTGACAAGGCTGGATCTTACAAGTGTG GACCCTGGGGGCCCAGTCAATGGGTACCAGAAAATAACAGGGGGCCCTGGGCTTATCAACGG ACGCCATGCTAAAATTGGCACCGTGGTGTCTTTCTTTTGTAACAACTCCTATGTTCTTAGTG GCAATGAGAAAAGAACTTGCCAGCAGAATGGAGAGTGGTCAGGGAAACAGCCCATCTGCATA **AAAGCCTGCCGAGAACCAAAGATTTCAGACCTGGTGAGAAGGAGAGTTCTTCCGATGCAGGT** AGAGTGCCCCTACCAAGAAGCCAGCCCTTCCCTTTGGAGATCTGCCCATGGGATACCAACAT CTGCATACCCAGCTCCAGTATGAGTGCATCTCACCCTTCTACCGCCGCCTGGGCAGCAGCAG GAGGACATGTCTGAGGACTGGGAAGTGGAGTGGGCGGCACCATCCTGCATCCCTATCTGCG ATCTACAGGAGGACCAGCGGGGTGCATGACGGCAGCCTACACAAGGGAGCGTGGTTCCTAGT CTGCAGCGGTGCCCTGGTGAATGAGCGCACTGTGGTGGTGGCTGCCCACTGTGTTACTGACC TGGGGAAGGTCACCATGATCAAGACAGCAGACCTGAAAGTTGTTTTGGGGAAATTCTACCGG GATGATGACCGGGATGAGAAGACCATCCAGAGCCTACAGATTTCTGCTATCATTCTGCATCC CAACTATGACCCCATCCTGCTTGATGCTGACATCGCCATCCTGAAGCTCCTAGACAAGGCCC CAGGAGTCCCACATCACTGTGGCTGGCTGGAATGTCCTGGCAGACGTGAGGAGCCCTGGCTT CAAGAACGACACTGCGCTCTGGGGTGGTCAGTGTGGTGGACTCGCTGTGTGAGGAGC **AGCATGAGGACCATGGCATCCCAGTGAGTGTCACTGATAACATGTTCTGTGCCAGCTGGGAA** CCCACTGCCCTTCTGATATCTGCACTGCAGAGACAGGAGGCATCGCGGCTGTGTCCTTCCC GGGACGACCATCTCCTGAGCCACGCTGGCATCTGATGGGACTGGTCAGCTGGAGCTATGATA **AAACATGCAGCCACAGGCTCTCCACTGCCTTCACCAAGGTGCTGCCTTTTAAAGACTGGATT** GAAAGAAATATGAAATGAACCATGCTCATGCACTCCTTGAGAAGTGTTTCTGTATATCCGTC TGTACGTGTGTCATTGCGTGAAGCAGTGTGGGCCTGAAGTGTGATTTGGCCTGTGAACTTGG CTGTGCCAGGGCTTCTGACTTCAGGGACAAAACTCAGTGAAGGGTGAGTAGACCTCCATTGC TGGTAGGCTGATGCCGCGTCCACTACTAGGACAGCCAATTGGAAGATGCCAGGGCTTGCAAG **AAGTAAGTTTCTTCAAAGAAGACCATATACAAAACCTCTCCACTCCACTGACCTGGTGGTCT** TCCCCAACTTTCAGTTATACGAATGCCATCAGCTTGACCAGGGAAGATCTGGGCTTCATGAG GCCCCTTTTGAGGCTCTCAAGTTCTAGAGAGCTGCCTGTGGGACAGCCCAGGGCAGCAGAGC

162/310 FIGURE 159

MELGCWTQLGLTFLQLLLISSLPREYTVINEACPGAEWNIMCRECCEYDQIECVCPGKREVV
GYTIPCCRNEENECDSCLIHPGCTIFENCKSCRNGSWGGTLDDFYVKGFYCAECRAGWYGGD
CMRCGQVLRAPKGQILLESYPLNAHCEWTIHAKPGFVIQLRFVMLSLEFDYMCQYDYVEVRD
GDNRDGQIIKRVCGNERPAPIQSIGSSLHVLFHSDGSKNFDGFHAIYEEITACSSSPCFHDG
TCVLDKAGSYKCACLAGYTGQRCENLLEERNCSDPGGPVNGYQKITGGPGLINGRHAKIGTV
VSFFCNNSYVLSGNEKRTCQQNGEWSGKQPICIKACREPKISDLVRRRVLPMQVQSRETPLH
QLYSAAFSKQKLQSAPTKKPALPFGDLPMGYQHLHTQLQYECISPFYRRLGSSRRTCLRTGK
WSGRAPSCIPICGKIENITAPKTQGLRWPWQAAIYRRTSGVHDGSLHKGAWFLVCSGALVNE
RTVVVAAHCVTDLGKVTMIKTADLKVVLGKFYRDDDRDEKTIQSLQISAIILHPNYDPILLD
ADIAILKLLDKARISTRVQPICLAASRDLSTSFQESHITVAGWNVLADVRSPGFKNDTLRSG
VVSVVDSLLCEEQHEDHGIPVSVTDNMFCASWEPTAPSDICTAETGGIAAVSFPGRASPEPR
WHLMGLVSWSYDKTCSHRLSTAFTKVLPFKDWIERNMK

FIGURE 160

ACCAGGCATTGTATCTTCAGTTGTCATCAAGTTCGCAATCAGATTGGAAAAGCTCAACTTGA AGCTTTCTTGCCTGCAGTGAAGCAGAGAGATAGATATTATTCACGTAATAAAAAACATGGGC TTCAACCTGACTTTCCACCTTTCCTACAAATTCCGATTACTGTTGCTGTTGACTTTGTGCCT GACAGTGGTTGGGTGGGCCACCAGTAACTACTTCGTGGGTGCCATTCAAGAGATTCCTAAAG CAAAGGAGTTCATGGCTAATTTCCATAAGACCCTCATTTTGGGGAAAGGGAAAAACTCTGACT **AATGAAGCATCCACGAAGAAGGTAGAACTTGACAACTGTCCTTCTGTGTCTCCTTACCTCAG** AGGCCAGAGCAAGCTCATTTTCAAACCAGATCTCACTTTGGAAGAGGTACAGGCAGAAAATC CCAAAGTGTCCAGAGGCCGGTATCGCCCTCAGGAATGTAAAGCTTTACAGAGGGTCGCCATCCTC GTTCCCCACCGGAACAGAGAAACACCTGATGTACCTGCTGGAACATCTGCATCCCTTCCT GCAGAGGCAGCAGCTGGATTATGGCATCTACGTCATCCACCAGGCTGAAGGTAAAAAGTTTA ATCGAGCCAAACTCTTGAATGTGGGCTATCTAGAAGCCCTCAAGGAAGAAATTGGGACTGC TTTATATTCCACGATGTGGACCTGGTACCCGAGAATGACTTTAACCTTTACAAGTGTGAGGA GCATCCCAAGCATCTGGTGGTTGGCAGGAACAGCACTGGGTACAGGTTACGTTACAGTGGAT ATTTTGGGGGTGTTACTGCCCTAAGCAGAGAGCAGTTTTTCAAGGTGAATGGATTCTCTAAC **AACTACTGGGGATGGGGAGGCGAAGACGATGACCTCAGACTCAGGGTTGAGCTCCAAAGAAT** GAAAATTTCCCGGCCCCTGCCTGAAGTGGGTAAATATACAATGGTCTTCCACACTAGAGACA AAGGCAATGAGGTGAACGCAGAACGGATGAAGCTCTTACACCAAGTGTCACGAGTCTGGAGA ACAGATGGGTTGAGTAGTTCTTATAAATTAGTATCTGTGGAACACAATCCTTTATATAT ${\tt CAACATCACAGTGGATTTCTGGTTTGGTGCA} \underline{{\tt TGA}} {\tt CCCTGGATCTTTTGGTGATGTTTGGAAG}$ AACTGATTCTTTGTTTGCAATAATTTTGGCCTAGAGACTTCAAATAGTAGCACACATTAAGA ACCTGTTACAGCTCATTGTTGAGCTGAATTTTTCCTTTTGTATTTTCTTAGCAGAGCTCCT GGTGATGTAGAGTATAAAACAGTTGTAACAAGACAGCTTTCTTAGTCATTTTGATCATGAGG GTTAAATATTGTAATATGGATACTTGAAGGACTTTATATAAAAGGATGACTCAAAGGATAAA GGGATAAAAGGCCACAGGAAATAAGACTGCTGAATGTCTGAGAGAACCAGAGTTGTTCTCGT CCAAGGTAGAAAGGTACGAAGATACAATACTGTTATTCATTTATCCTGTACAATCATCTGTG AAGTGGTGGTGTCAGGTGAGAAGGCGTCCACAAAAGAGGGGAGAAAAGGCGACGAATCAGGA CACAGTGAACTTGGGAATGAAGAGGTAGCAGGAGGGTGGAGTGTCGGCTGCAAAGGCAGCAG TAGCTGAGCTGGTTGCAGGTGCTGATAGCCTTCAGGGGAGGACCTGCCCAGGTATGCCTTCC AGTGATGCCCACCAGAGAATACATTCTCTATTAGTTTTTAAAGAGTTTTTGTAAAATGATTT CTATCAAATACCTCTGTAGTAAAATGTGAAAAAGCAAAA

ر (4/510 FIGURE 161

MGFNLTFHLSYKFRLLLLLTLCLTVVGWATSNYFVGAIQEIPKAKEFMANFHKTLILGKGKT
LTNEASTKKVELDNCPSVSPYLRGQSKLIFKPDLTLEEVQAENPKVSRGRYRPQECKALQRV
AILVPHRNREKHLMYLLEHLHPFLQRQQLDYGIYVIHQAEGKKFNRAKLLNVGYLEALKEEN
WDCFIFHDVDLVPENDFNLYKCEEHPKHLVVGRNSTGYRLRYSGYFGGVTALSREQFFKVNG
FSNNYWGWGGEDDDLRLRVELQRMKISRPLPEVGKYTMVFHTRDKGNEVNAERMKLLHQVSR
VWRTDGLSSCSYKLVSVEHNPLYINITVDFWFGA

Important features:

Signal peptide:

amino acids 1-27

N-glycosylation sites:

amino acids 4-7, 220-223 and 335-338

Xylose isomerase proteins:

amino acids 191-201

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CGTGGGCCGGGTCGCGCGGGGGCTGTGGGCGCGCCGCAGGAGCGACCGCCGCAGTTCTC GAGCTCCAGCTGCATTCCCTCCGCGTCCGCCCCACGCTTCTCCCGCTCCGGGCCCCGCAATG CCCGGCAGGGTGGCCGCAGGCCTGTATGAACTCAATCTCACCACCGATAGCCCTGCCACCA CGGGAGCGGTGGTCACCATCTCGGCCAGCCTGGTGGCCAAGGACAACGGCAGCCTGGCCCTG CCCGCTGACGCCCACCTCTACCGCTTCCACTGGATCCACACCCCGCTGGTGCTTACTGGCAA GATGGAGAAGGGTCTCAGCTCCACCATCCGTGTGGTCGGCCACGTGCCCGGGGAATTCCCGG TCTCTGTCTGGGTCACTGCCGCTGACTGCTGGATGTGCCAGCCTGTGGCCAGGGGCTTTGTG GTCCTCCCCATCACAGAGTTCCTCGTGGGGGACCTTGTTGTCACCCCAGAACACTTCCCTACC GCAACTTCCTCAAGACCGCCTTGTTTCTCTACAGCTGGGACTTCGGGGACCGGGACCCAGATG GTGACTGAAGACTCCGTGGTCTATTATAACTATTCCATCATCGGGACCTTCACCGTGAAGCT CAAAGTGGTGGCGGAGTGGGAAGAGGTGGAGCCGGATGCCACGAGGGCTGTGAAGCAGAAGA CCGGGGACTTCTCCGCCTCGCTGAAGCTGCAGGAAACCCTTCGAGGCATCCAAGTGTTGGGG CCCACCTAATTCAGACCTTCCAAAAGATGACCGTGACCTTGAACTTCCTGGGGAGCCCTCC TCTGACTGTGTGCTGGCGTCTCAAGCCTGAGTGCCTCCCGCTGGAGGAAGGGGAGTGCCACC CTGTGTCCGTGGCCAGCACAGCGTACAACCTGACCCACACCTTCAGGGACCCTGGGGACTAC TGCTTCAGCATCCGGGCCGAGAATATCATCAGCAAGACACATCAGTACCACAAGATCCAGGT GTGGCCCTCCAGAATCCAGCCGGCTGTCTTTGCTTTCCCATGTGCTACACTTATCACTGTGA TGTTGGCCTTCATCATGTACATGACCCTGCGGAATGCCACTCAGCAAAAGGACATGGTGGAG AACCCGGAGCCACCCTCTGGGGTCAGGTGCTGCTGCCAGATGTGCTGTGGGCCTTTCTTGCT ATAAGTCTGTCAAAACTTACACCGTG<u>TGA</u>GCACTCCCCCTCCCCACCCCATCTCAGTGTTAA CTGACTGCTGACTTGGAGTTTCCAGCAGGGTGGTGTGCACCACTGACCAGGAGGGGTTCATT TGCGTGGGCTGTTGGCCTGGATCATCCATCTGTACAGTTCAGCCACTGCCACAAGCC CCTCCCTCTCTGTCACCCCTGACCCCAGCCATTCACCCATCTGTACAGTCCAGCCACTGACA TAAGCCCCACTCGGTTACCACCCCCTTGACCCCCTACCTTTGAAGAGGCTTCGTGCAGGACT TTGATGCTTGGGGTGTTCCGTGTTGACTCCTAGGTGGGCCTGGCTGCCCACTGCCCATTCCT CTCATATTGGCACATCTGCTGTCCATTGGGGGTTCTCAGTTTCCTCCCCCAGACAGCCCTAC CTGTGCCAGAGAGCTAGAAAGAGGTCATAAAGGGTTAAAAATCCATAACTAAAGGTTGTAC CACACACACAGAAATATAAACACATGCGTCACATGGGCATTTCAGATGATCAGCTCTGTA TCTGGTTAAGTCGGTTGCTGGGATGCACCCTGCACTAGAGCTGAAAGGAAATTTGACCTCCA AGCAGCCCTGACAGGTTCTGGGCCCGGGCCCTCCCTTTGTGCTTTGTCTCTGCAGTTCTTGC GCCCTTTATAAGGCCATCCTAGTCCCTGCTGGCTGGCAGGGGCCTGGATGGGGGGCAGGACT AATACTGAGTGATTGCAGAGTGCTTTATAAATATCACCTTATTTTATCGAAACCCATCTGTG AAACTTTCACTGAGGAAAAGGCCTTGCAGCGGTAGAAGAGGTTGAGTCAAGGCCGGGCGCGC TGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGTGGATCACGAGATCAGGA GATCGAGACCACCCTGGCTAACACGGTGAAACCCCGTCTCTACTAAAAAAATACAAAAAGTT AGCCGGGCGTGGTGGTGCCTGTAGTCCCAGCTACTCGGGAGGCTGAGGCAGGAGAATG GTGCGAACCCGGGAGGCGGAGCTTGCAGTGAGCCCAGATGGCGCCACTGCACTCCAGCCTGA GTGACAGAGCGAGACTCTGTCTCCA

مر 66/310 FIGURE 163

MAQAVWSRLGRILWLACLLPWAPAGVAAGLYELNLTTDSPATTGAVVTISASLVAKDNGSLA
LPADAHLYRFHWIHTPLVLTGKMEKGLSSTIRVVGHVPGEFPVSVWVTAADCWMCQPVARGF
VVLPITEFLVGDLVVTQNTSLPWPSSYLTKTVLKVSFLLHDPSNFLKTALFLYSWDFGDGTQ
MVTEDSVVYYNYSIIGTFTVKLKVVAEWEEVEPDATRAVKQKTGDFSASLKLQETLRGIQVL
GPTLIQTFQKMTVTLNFLGSPPLTVCWRLKPECLPLEEGECHPVSVASTAYNLTHTFRDPGD
YCFSIRAENIISKTHQYHKIQVWPSRIQPAVFAFPCATLITVMLAFIMYMTLRNATQQKDMV
ENPEPPSGVRCCCQMCCGPFLLETPSEYLEIVRENHGLLPPLYKSVKTYTV

Important features of the protein: Signal peptide:

amino acids 1-24

Transmembrane domain:

amino acids 339-362

N-glycosylation sites.

amino acids 34-37, 58-61, 142-145, 197-200, 300-303 and 364-367

167/510

FIGURE 164

168/210 FIGURE 165

MALSSQIWAACLLLLLLLASLTSGSVFPQQTGQLAELQPQDRAGARASWMPMFQRRRRDTH FPICIFCCGCCHRSKCGMCCKT

برد کاری FIGURE 166

CTGTCAGGAAGGACCATCTGAAGGCTGCAATTTGTTCTTAGGGAGGCAGGTGCTGGCCTGGC CTGGATCTTCCACC<u>ATG</u>TTCCTGTTGCTGCCTTTTGATAGCCTGATTGTCAACCTTCTGGGC AGTCTCCTTTGGTATCCGCAAACTCTACATGAAAAGTCTGTTAAAAATCTTTGCGTGGGCTA CCTTGAGAATGGAGCGAGGAGCCAAGGAGAAGAACCACCAGCTTTACAAGCCCTACACCAAC GGAATCATTGCAAAGGATCCCACTTCACTAGAAGAAGAGATCAAAGAGATTCGTCGAAGTGG TAGTAGTAAGGCTCTGGACAACACTCCAGAGTTCGAGCTCTCTGACATTTTCTACTTTTGCC GGAAAGGAATGGAGACCATTATGGATGATGAGGTGACAAAGAGATTCTCAGCAGAAGAACTG GAGTCCTGGAACCTGCTGAGCAGAACCAATTATAACTTCCAGTACATCAGCCTTCGGCTCAC GGTCCTGTGGGGGTTAGGAGTGCTGATTCGGTACTGCTTTCTGCTGCCGCTCAGGATAGCAC TGGCTTTCACAGGGATTAGCCTTCTGGTGGTGGGCACAACTGTGGTGGGATACTTGCCAAAT AGCGCTGACAGCCATCATCACCTACCATGACAGGGAAAACAGACCAAGAAATGGTGGCATCT GTGTGGCCAATCATACCTCACCGATCGATGTGATCATCTTGGCCAGCGATGGCTATTATGCC ATGGTGGGTCAAGTGCACGGGGGACTCATGGGTGTGATTCAGAGAGCCCATGGTGAAGGCCTG CCCACACGTCTGGTTTGAGCGCTCGGAAGTGAAGGATCGCCACCTGGTGGCTAAGAGACTGA CTGAACATGTGCAAGATAAAAGCAAGCTGCCTATCCTCATCTTCCCAGAAGGAACCTGCATC AATAATACATCGGTGATGATGTTCAAAAAGGGAAGTTTTGAAATTGGAGCCACAGTTTACCC TGTTGCTATCAAGTATGACCCTCAATTTGGCGATGCCTTCTGGAACAGCAGCAAATACGGGA TGGTGACGTACCTGCGAATGATGACCAGCTGGGCCATTGTCTGCAGCGTGTGGTACCTG CCTCCCATGACTAGAGAGGCAGATGAAGATGCTGTCCAGTTTGCGAATAGGGTGAAATCTGC CATTGCCAGGCAGGAGGACTTGTGGACCTGCTGTGGGATGGGGGCCTGAAGAGGGAGAAGG TGAAGGACACGTTCAAGGAGGAGCAGCAGAAGCTGTACAGCAAGATGATCGTGGGGAACCAC AAGGACAGGAGCCGCTCC<u>TGA</u>GCCTGCCTCCAGCTGGCTGGGGCCCACCGTGCGGGGTGCCAA CGGGCTCAGAGCTGGAGTTGCCGCCGCCGCCCCCACTGCTGTCCTTTCCAGACTCCAGGG CTCCCCGGGCTGCTCTGGATCCCAGGACTCCGGCTTTCGCCGAGCCGCAGCGGGATCCCTGT GCACCCGGCGCAGCCTACCCTTGGTGGTCTAAACGGATGCTGCTGGGTGTTGCGACCCAGGA CGAGATGCCTTGTTTCTTTTACAATAAGTCGTTGGAGGAATGCCATTAAAGTGAACTCCCCA CCTTTGCACGCTGTGCGGGCTGAGTGGTTGGGGAGATGTGGCCATGGTCTTGTGCTAGAGAT GGCGGTACAAGAGTCTGTTATGCAAGCCCGTGTGCCAGGGATGTGCTGGGGGGCGCCCACCCG CTCTCCAGGAAAGGCACAGCTGAGGCACTGTGGCTGGCTTCGGCCTCAACATCGCCCCCAGC CTTGGAGCTCTGCAGACATGATAGGAAGGAAACTGTCATCTGCAGGGGCTTTCAGCAAAATG GGCCGCTGACTGGGCCATGGGGAGAACGTGTGTTCGTACTCCAGGCTAACCCTGAACTCCCC **ATGTGATGCGCGCTTTGTTGAATGTGTGTCTCGGTTTCCCCATCTGTAATATGAGTCGGGGG** AGGACACATCACGTTCAGTGTTTCAAGTACAGGCCCACAAAAGGGGGCACGGCAGGCCTGAG

MFLLLPFDSLIVNLLGISLTVLFTLLLVFIIVPAIFGVSFGIRKLYMKSLLKIFAWATLRME
RGAKEKNHQLYKPYTNGIIAKDPTSLEEEIKEIRRSGSSKALDNTPEFELSDIFYFCRKGME
TIMDDEVTKRFSAEELESWNLLSRTNYNFQYISLRLTVLWGLGVLIRYCFLLPLRIALAFTG
ISLLVVGTTVVGYLPNGRFKEFMSKHVHLMCYRICVRALTAIITYHDRENRPRNGGICVANH
TSPIDVIILASDGYYAMVGQVHGGLMGVIQRAMVKACPHVWFERSEVKDRHLVAKRLTEHVQ
DKSKLPILIFPEGTCINNTSVMMFKKGSFEIGATVYPVAIKYDPQFGDAFWNSSKYGMVTYL
LRMMTSWAIVCSVWYLPPMTREADEDAVQFANRVKSAIARQGGLVDLLWDGGLKREKVKDTF
KEEQQKLYSKMIVGNHKDRSRS

ペキュ/300 FIGURE 168

GCCCTCGAAACCAGGACTCCAGCACCTCTGGTCCCGCCCTCACCCGGACCCCTGGCCCTCA CGTCTCCTCCAGGGATGGCGCTGGCGGCTTTGATGATCGCCCTCGGCAGCCTCGGCCTCCAC ACCTGGCAGGCCCAGGCTGTTCCCACCATCCTGCCCCTGGGCCTGGCTCCAGACACCTTTGA CGATACCTATGTGGGTTGTGCAGAGGGGGAGAGGGAGAGGCCCCCCTGCTAAAGGAGG AAATGGCCCACCATGCCTGCTGCGGGAATCCTGGGAGGCAGCCCAGGAGACCTGGGAGGAC AAGCGTCGAGGGCTTACCTTGCCCCCTGGCTTCAAAGCCCAGAATGGAATAGCCATTATGGT CTACACCAACTCATCGAACACCTTGTACTGGGAGTTGAATCAGGCCGTGCGGACGGGCGGAG GCTCCCGGGAGCTCTACATGAGGCACTTTCCCTTCAAGGCCCTGCATTCTACCTGATCCGG GCCTGCAGCTGCTGCGAGGCAGTGGGGGGCTGCAGCAGGGGACCTGGGGAGGTGTTTCCG AGGTGTGGGCAGCCTTCGCTTTGAACCCAAGAGGCTGGGGGACTCTGTCCGCTTGGGCCAGT TTGCCTCCAGCTCCCTGGATAAGGCAGTGGCCCACAGATTTGGGGAGAAGAGGCGGGGCTGT GTGTCTGCGCCAGGGGTGCAGCTAGGGTCACAATCTGAGGGGGCCTCCTCTCTGCCCCCCTG GAAGACTCTGCTCTTGGCCCCTGGAGAGTTCCAGCTCTCAGGGGTTGGGCCC<u>TGA</u>AAGTCCA ACATCTGCCACTTAGGAGCCCTGGGAACGGGTGACCTTCATATGACGAAGAGGCACCTCCAG CAGCCTTGAGAAGCAAGAACATGGTTCCGGACCCAGCCCTAGCAGCCTTCTCCCCAACCAGG ATGTTGGCCTGGGGAGGCCACAGCAGGGCTGAGGGAACTCTGCTATGTGATGGGGACTTCCT

TGGAGTTTTATTGAGGTAGCTACGTGATTAAATGGTATTGCAGTGTGGA

メギとかい FIGURE 169

MALAALMIALGSLGLHTWQAQAVPTILPLGLAPDTFDDTYVGCAEEMEEKAAPLLKEEMAHH ALLRESWEAAQETWEDKRRGLTLPPGFKAQNGIAIMVYTNSSNTLYWELNQAVRTGGGSREL YMRHFPFKALHFYLIRALQLLRGSGGCSRGPGEVVFRGVGSLRFEPKRLGDSVRLGQFASSS LDKAVAHRFGEKRRGCVSAPGVQLGSQSEGASSLPPWKTLLLAPGEFQLSGVGP

→₹3/310 **FIGURE 170**

GTGGCTTCATTTCAGTGGCTGACTTCCAGAGAGCAATATGGCTGGTTCCCCAACATGCCTCA CCCTCATCTATATCCTTTGGCAGCTCACAGGGTCAGCAGCCTCTGGACCCGTGAAAGAGCTG GTCGGTTCCGTTGGTGGGCCGTGACTTTCCCCCTGAAGTCCAAAGTAAAGCAAGTTGACTC TATTGTCTGGACCTTCAACACCCCTCTTGTCACCATACAGCCAGAAGGGGGCACTATCA TAGTGACCCAAAATCGTAATAGGGAGAGAGTAGACTTCCCAGATGGAGGCTACTCCCTGAAG CTCAGCAAACTGAAGAAGAATGACTCAGGGATCTACTATGTGGGGATATACAGCTCATCACT CCAGCAGCCCTCCACCCAGGAGTACGTGCTGCATGTCTACGAGCACCTGTCAAAGCCTAAAG TCACCATGGGTCTGCAGAGCAATAAGAATGGCACCTGTGTGACCAATCTGACATGCTGCATG GAACATGGGGAAGAGGATGTGATTTATACCTGGAAGGCCCTGGGGCAAGCAGCCAATGAGTC CCATAATGGGTCCATCCTCCCCATCTCCTGGAGATGGGGGAGAAGTGATATGACCTTCATCT GCGTTGCCAGGAACCCTGTCAGCAGAAACTTCTCAAGCCCCATCCTTGCCAGGAAGCTCTGT GAAGGTGCTGATGACCCAGATTCCTCCATGGTCCTCCTGTGTCTCCTGTTGGTGCCCCT AGTACATTGAAGAGAAGAGAGAGTGGACATTTGTCGGGAAACTCCTAACATATGCCCCCAT TCTGGAGAGAACACAGAGTACGACACAATCCCTCACACTAATAGAACAATCCTAAAGGAAGA TCCAGCAAATACGGTTTACTCCACTGTGGAAATACCGAAAAAGATGGAAAATCCCCACTCAC TGCTCACGATGCCAGACACACCAAGGCTATTTGCCTATGAGAATGTTATCTAGACAGCAGTG

CACTCCCCTAAGTCTCTGCTCA

174/510 FIGURE 171

MAGSPTCLTLIYILWQLTGSAASGPVKELVGSVGGAVTFPLKSKVKQVDSIVWTFNTTPLVT
IQPEGGTIIVTQNRNRERVDFPDGGYSLKLSKLKKNDSGIYYVGIYSSSLQQPSTQEYVLHV
YEHLSKPKVTMGLQSNKNGTCVTNLTCCMEHGEEDVIYTWKALGQAANESHNGSILPISWRW
GESDMTFICVARNPVSRNFSSPILARKLCEGAADDPDSSMVLLCLLLVPLLLSLFVLGLFLW
FLKRERQEEYIEEKKRVDICRETPNICPHSGENTEYDTIPHTNRTILKEDPANTVYSTVEIP
KKMENPHSLLTMPDTPRLFAYENVI

ペキ5/パロ FIGURE 172

CTGGTTCCCCAACATGCCTCACCTCATCTATATCCTTTGGCAGCTCACAGGGTCAGCAGCC TCTGGACCCGTGAAAGAGCTGGTCGGTTCCGTTGGTGGGCCCGTGACTTTCCCCCTGAAGTC CAAAGTAAAGCAAGTTGACTCTATTGTCTGGACCTTCAACACACCCCTCTTGTCACCATAC AGCCAGAAGGGGGCACTATCATAGTGACCCAAAATCGTAATAGGGAGAGAGTAGACTTCCCA GATGGAGGCTACTCCCTGAAGCTCAGCAAACTGAAGAAGAATGACTCAGGGATCTACTATGT GGGGATATACAGCTCATCACTCCAGCAGCCCCTCCACCCAGGAGTACGTGCTGCATGTCTACG AGCACCTGTCAAAGCCTAAAGTCACCATGGGTCTGCAGAGCAATAAGAATGGCACCTGTGTG ACCAATCTGACATGCTGCATGGAACATGGGGAAGAGGTGATTTATACCTGGAAGGCCCT GGGGCAAGCAGCCAATGAGTCCCATAATGGGTCCATCCTCCCCATCTCCTGGAGATGGGGAG AAAGTGATATGACCTTCATCTGCGTTGCCAGGAACCCTGTCAGCAGAAACTTCTCAAGCCCC ATCCTTGCCAGGAAGCTCTGTGAAGGTGCTGCTGATGACCCAGATTCCTCCATGGTCCTCCT GTGTCTCCTGTTGGTGCCCCTCCTGCTCAGTCTCTTTGTACTGGGGCTATTTCTTTGGTTTC ACTCCTAACATATGCCCCCATTCTGGAGAGAACACAGAGTACGACAAATCCCTCACACTAA TAGAACAATCCTAAAGGAAGATCCAGCAAATACGGTTTACTCCACTGTGGAAATACCGAAAA AGATGGAAAATCCCCACTCACTGCTCACGATGCCAGACACCAAGGCTATTTGCCTATGAG

-176/310 FIGURE 173

_**/3\0 **FIGURE 174**

MKMLLLLCLGLTLVCVHAEEASSTGRNFNVEKINGEWHTIILASDKREKIEEHGNFRLFLEQ IHVLENSLVLKVHTVRDEECSELSMVADKTEKAGEYSVTYDGFNTFTIPKTDYDNFLMAHLI NEKDGETFQLMGLYGREPDLSSDIKERFAQLCEEHGILRENIIDLSNANRCLQARE

178/310

FIGURE 175

__\¥9/>\0 FIGURE 176

MTCCEGWTSCNGFSLLVLLLLGVVLNAIPLIVSLVEEDQFSQNPISCFEWWFPGIIGAGLMA IPATTMSLTARKRACCNNRTGMFLSSFFSVITVIGALYCMLISIQALLKGPLMCNSPSNSNA NCEFSLKNISDIHPESFNLQWFFNDSCAPPTGFNKPTSNDTMASGWRASSFHFDSEENKHRL IHFSVFLGLLLVGILEVLFGLSQIVIGFLGCLCGVSKRRSQIV

GTCGAATCCAAATCACTCATTGTGAAAGCTGAGCTCACAGCCGAATAAGCCACCATGAGGCT
GTCAGTGTGTCTCCTGATGGTCTCGCTGGCCCTTTGCTGCTACCAGGCCCATGCTCTTGTCT
GCCCAGCTGTTGCTTCTGAGATCACAGTCTTCTTATTCTTAAGTGACGCTGCGGTAAACCTC
CAAGTTGCCAAACTTAATCCACCTCCAGAAGCTCTTGCAGCCAAGTTGGAAGTGAAGCACTG
CACCGATCAGATATCTTTTAAGAAACGACTCTCATTGAAAAAAGTCCTGGTGGAAA<u>TAG</u>TGAA
AAAATGTGGTGTGTGACATGTAAAAATGCTCAACCTGGTTTCCAAAGTCTTTCAACGACACC

18:4/310 FIGURE 178

MRLSVCLLMVSLALCCYQAHALVCPAVASEITVFLFLSDAAVNLQVAKLNPPPEALAAKLEV KHCTDQISFKKRLSLKKSWWK

→83/310 **FIGURE 180**

MERVTLALLLLAGLTALEANDPFANKDDPFYYDWKNLQLSGLICGGLLAIAGIAAVLSGKCK YKSSOKQHSPVPEKAIPLITPGSATTC

184/310 FIGURE 181

GGAGAAGAGGTTGTGTGGGACAAGCTGCTCCCGACAGAAGG<u>ATG</u>TCGCTGCTGAGCCTGCCC TGGCTGGGCCTCAGACCGGTGGCAATGTCCCCATGGCTACTCCTGCTGCTGGTTGTGGGCTC CTGGCTACTCGCCCGCATCCTGGCTTGGACCTATGCCTTCTATAACAACTGCCGCCGGCTCC AGTGTTTCCCACAGCCCCCAAAACGGAACTGGTTTTGGGGTCACCTGGGCCTGATCACTCCT ACAGAGGGGCTTGAAGGACTCGACCCAGATGTCGGCCACCTATTCCCAGGGCTTTACGGT ATGGCTGGGTCCCATCATCCCCTTCATCGTTTTATGCCACCCTGACACCATCCGGTCTATCA CCAATGCCTCAGCTGCCATTGCACCCAAGGATAATCTCTTCATCAGGTTCCTGAAGCCCTGG CTGGGAGAAGGGATACTGCTGAGTGGCGGTGACAAGTGGAGCCGCCACCGTCGGATGCTGAC GCCCGCCTTCCATTTCAACATCCTGAAGTCCTATATAACGATCTTCAACAAGAGTGCAAACA TCATGCTTGACAAGTGGCAGCACCTGGCCTCAGAGGGCAGCAGTCGTCTGGACATGTTTGAG CACATCAGCCTCATGACCTTGGACAGTCTACAGAAATGCATCTTCAGCTTTGACAGCCATTG TCAGGAGAGGCCCAGTGAATATATTGCCACCATCTTGGAGCTCAGTGCCCTTGTAGAGAAAA GAAGCCAGCATATCCTCCAGCACATGGACTTTCTGTATTACCTCTCCCATGACGGCGCGC TTCCACAGGGCCTGCCGCCTGGTGCATGACTTCACAGACGCTGTCATCCGGGAGCGGCGTCG CACCCTCCCCACTCAGGGTATTGATGATTTTTTCAAAGACAAAGCCAAGTCCAAGACTTTGG ATTTCATTGATGTGCTTCTGCTGAGCAAGGATGAAGATGGGAAGGCATTGTCAGATGAGGAT ATAAGAGCAGAGGCTGACACCTTCATGTTTGGAGGCCATGACACCACGGCCAGTGGCCTCTC CTGGGTCCTGTACAACCTTGCGAGGCACCCAGAATACCAGGAGCGCTGCCGACAGGAGGTGC AAGAGCTTCTGAAGGACCGCGATCCTAAAGAGATTGAATGGGACGACCTGGCCCAGCTGCCC TTCCTGACCATGTGCGTGAAGGAGGCCTGAGGTTACATCCCCCAGCTCCCTTCATCTCCCG ATGCTGCACCCAGGACATTGTTCTCCCAGATGGCCGAGTCATCCCCAAAGGCATTACCTGCC TCATCGATATTATAGGGGTCCATCACAACCCAACTGTGTGGCCGGATCCTGAGGTCTACGAC CCCTTCCGCTTTGACCCAGAGAACAGCAAGGGGAGGTCACCTCTGGCTTTTATTCCTTTCTC CGCAGGGCCCAGGAACTGCATCGGGCAGGCGTTCGCCATGGCGGAGATGAAAGTGGTCCTGG CGTTGATGCTGCACTTCCGGTTCCTGCCAGACCACACTGAGCCCCGCAGGAAGCTGGAA $G\underline{TGA}$ CTTTCTGACCCATCCACCTGTTTTTTTGCAGATTGTCATGAATAAAACGGTGCTGTCAAA

→85/310 FIGURE 182

MSLLSLPWLGLRPVAMSPWLLLLLVVGSWLLARILAWTYAFYNNCRRLQCFPQPPKRNWFWG
HLGLITPTEEGLKDSTQMSATYSQGFTVWLGPIIPFIVLCHPDTIRSITNASAAIAPKDNLF
IRFLKPWLGEGILLSGGDKWSRHRRMLTPAFHFNILKSYITIFNKSANIMLDKWQHLASEGS
SRLDMFEHISLMTLDSLQKCIFSFDSHCQERPSEYIATILELSALVEKRSQHILQHMDFLYY
LSHDGRRFHRACRLVHDFTDAVIRERRRTLPTQGIDDFFKDKAKSKTLDFIDVLLLSKDEDG
KALSDEDIRAEADTFMFGGHDTTASGLSWVLYNLARHPEYQERCRQEVQELLKDRDPKEIEW
DDLAQLPFLTMCVKESLRLHPPAPFISRCCTQDIVLPDGRVIPKGITCLIDIIGVHHNPTVW
PDPEVYDPFRFDPENSKGRSPLAFIPFSAGPRNCIGQAFAMAEMKVVLALMLLHFRFLPDHT
EPRRKLELIMRAEGGLWLRVEPLNVGLQ

→8₹/>\° FIGURE 184

 ${\tt MYKLASCCLLFTGFLNPLLSLPLLDSREISFQLSAPHEDARLTPEELERASLLQILPEMLGA} \\ {\tt ERGDILRKADSSTNIFNPRGNLRKFQDFSGQDPNILLSHLLARIWKPYKKRETPDCFWKYCV} \\$

188/310

FIGURE 185

FIGURE 186

 ${\tt MPSPGTVCSLLLLGMLWLDLAMAGSSFLSPEHQRVQQRKESKKPPAKLQPRALAGWLRPEDG}$ ${\tt GQAEGAEDELEVRFNAPFDVGIKLSGVQYQQHSQALGKFLQDILWEEAKEAPADKO}$

CGGCCACAGCTGGCATGCTCTGCCTGATCGCCATCCTGCTGTATGTCCTCGTCCAGTACCTC GTGAACCCCGGGGTGCTCCGCACGGACCCCAGATGTCAAGAAT<u>ATG</u>AACACGTGGCTGCTGT TCCTCCCCCTGTTCCCGGTGCAGGTGCAGACCCTGATAGTCGTGATCATCGGGATGCTCGTG $\tt CTCCTGCTGGACTTTCTTGGCTTGGTGCACCTGGGCCAGCTGCTCATCTTCCACATCTACCT$ GAGTATGTCCCCCACCCTAAGCCCCCGATCCCCCAAGGCTGGGTGGTCAGAGCTGCTCATC TTACACCTCTACTTGAGTATGTCCCTAACCCTGAGCCCCCACGCCTGGGGCCAGAGTCTTT GTCCCCCGTGTGCGCATGTGTTCAGGGTCAGCCTCTCCCAGAAGTGAGATCATGGACAAAAA GGGCAAATCACAGGAAGAAATTAAATCCATGAGGACCCAGCAGGCCCAGCAAGAAGCTGAAC GACAATGGAATGGAATCTATTAGGCAAGAACAGGACATTATGAAATAAGGACAGGTGGACTT AACAACTGAAGCGAGAGCTGTGGTCTTGCTTGGTCTCACAGTGGGCACAGCGGTAGGCGGTC AGTCATGTTGCTGAACGACGGAGGGTAAACTCCCCAGCCCCAAGAAAACCTGTGTTGGAAGT AACAACAACCTCCCTGCTCCTGGCACCAGCCGTTTTGGTCATGGTGGGCCAGCTGCAAAGCG ACGGGCAGCAGAGTGTGTCCAGGCCAGCCCCCAAGAATGCCCTGCTCCTGACAGCTTGGCCA ACCCCTGGTCAGGGCAGAGGGAGTTGGGTGGGTCAGGCTCTGGGCTCACCTCCATCTCCAGA GCATCCCCTGCCTGCAGTTGTGGCAAGAACGCCCAGCTCAGAATGAACACACCCCACCAAGA GCCTCCTTGTTCATAACCACAGGTTACCCTACAAACCACTGTCCCCACACAACCCTGGGGAT GTTTTAAAACACACCTCTAACGCATATCTTACAGTCACTGTTGTCTTGCCTGAGGGTTGA ATTTTTTTTAATGAAAGTGCAATGAAAATCACTGGATTAAATCCTACGGACACAGAGCTGAA **АКАКАКАКАКАКАКАКАКАКАКАКАК**

194/310 FIGURE 188

 ${\tt MNTWLLFLPLFPVQVQTLIVVIIGMLVLLLDFLGLVHLGQLLIFHIYLSMSPTLSPRSPQGW}$ VVRAAHLTPLLEYVPNPEPPTPGARVFVPRVRMCSGSASPRSEIMDKKGKSQEEIKSMRTQQ AQQEAELTPRPAGVVPGA

ام 22/30 FIGURE 189

GGAGTGCAGATGGCATCCTTCGGTTCTTCCAGACAAGCTGCAAGACGCTGACC<u>ATG</u>GCCAAG ATGGAGCTCTCGAAGGCCTTCTCTGGCCAGCGGACACTCCTATCTGCCATCCTCAGCATGCT ATCACTCAGCTTCTCCACAACATCCCTGCTCAGCAACTACTGGTTTGTGGGCACACAGAAGG TGCCCAAGCCCCTGTGCGAGAAAGGTCTGGCAGCCAAGTGCTTTGACATGCCAGTGTCCCTG GATGGAGATACCAACACCCCACCCAGGAGGTGGTACAATACAACTGGGAGACTGGGGATGA CCGGTTCTCCTTCCGGAGCTTCCGGAGTGGCATGTGGCTATCCTGTGAGGAAACTGTGGAAG GGACTACTGGAATTTGCCACGTTGCAAGGCCCATGTCACCCCACTCTCCGATTTGGAGGGAA GCGGTTGATGGAGAAGGCTTCCCTCCCCTCCCTTGGGGGCTTTGTGGCAAAAATCCTA TGGTTATCCCTGGGAACGCAGATCACCTACATCGGACTTCAATTCATCAGCTTCCTCCTGCT ACTAACAGACTTGCTACTCACTGGGAACCCTGCCTGTGGGCTCAAACTGAGCGCCTTTGCTG CTGTTTCCTCTGTCCTGTCAGGTCTCCTGGGGATGGTGGCCCACATGATGTATTCACAAGTC TTCCAAGCGACTGTCAACTTGGGTCCAGAAGACTGGAGACCACATGTTTGGAATTATGGCTG GGCCTTCTACATGGCCTGGCTCTCCTTCACCTGCTGCATGGCGTCGGCTGTCACCACCTTCA ACACGTACACCAGGATGGTGCTGGAGTTCAAGTGCAAGCA<u>TAG</u>TAAGAGCTTCAAGGAAAAC CCGAACTGCCTACCACATCACCATCAGTGTTTCCCTCGGCGGCTGTCAAGTGCAGCCCCCAC CGTGGGTCCTTTGACCAGCTACCACCAGTATCATAATCAGCCCATCCACTCTGTCTCTGAGG AAAGAAGCAGTTAGGTCATCTGTAGAGGAAGAGCAGTGTTAGGAGTTAAGCGGGTTTGGGGA GTAGGCTTGAGCCCTACCTTACACGTCTGCTGATTATCAACATGTGCTTAAGCCAACATCCG TCTCTTGAGCATGGTTTTTAGAGGCTACGAATAAGGCTATGAATAAGGGTTATCTTTAAGTC CTAAGGGATTCCTGGGTGCCACTGCTCTTTTCCTCTACAGCTCCATCTTGTTTCACCCAC ${\tt CCCACATCTCACACATCCAGAATTCCCTTCTTTACTGATAGTTTCTGTGCCAGGTTCTGGGC}$ TAAACCATGGAGATAAAAAGAAGAGTAAAATACACTTCCCGACCTTAAGGATCTGAAA

رير FIGURE 190

MAKMELSKAFSGQRTLLSAILSMLSLSFSTTSLLSNYWFVGTQKVPKPLCEKGLAAKCFDMP VSLDGDTNTSTQEVVQYNWETGDDRFSFRSFRSGMWLSCEETVEEPGERCRSFIELTPPAKR GEKGLLEFATLQGPCHPTLRFGGKRLMEKASLPSPPLGLCGKNPMVIPGNADHLHRTSIHQL PPATNRLATHWEPCLWAQTERLCCCFLCPVRSPGDGGPHDVFTSLPSDCQLGSRRLETTCLE LWLGLLHGLALLHLLHGVGCHHLQHVHQDGAGVQVQA

ر المراري FIGURE 191

AACTGGAAGGAAAGAAAGAAAGGTCAGCTTTGGCCCAGATGTGGTTACCCCTTGGTCTCCTG TCTTTATGTCTTCTCCTCTTCCTATTCTGTCATCTCCCTCACTTAAGTCTCAGGCCTGTCA GCAGCTCCTGTGGACATTGCCATCCCCTCTGGTAGCCTTCAGAGCAAACAGGACAACCTATG TTATGGATGTTTCCACCAACCAGGGTAGTGGCATGGAGCACCGTAACCATCTGTGCTTCTGT GATCTCTATGACAGAGCCACTTCTCCACCTCTGAAATGTTCCCTGCTCTGAAATCTGGCATG GTCTGTTCTCTTATTGTCAACCTCAGCACAACAGGCTGGCGCCAATGGCATTACAGAGAAAG CAATCTGTGTGGCTAGTGGGCAGATTACCATGCAAGCCCCAGGAGAAATGGAGGAGCTTTGT AGCCACCTCCCTGTCAGCCAGTATTAACATGTCCCCTTCCCCCTGCCCCGCCGTAGATTCAG GACATTCGCCCCTGTGTGCCACCAAACCAGGACTTTCCCCTTGGCTTGGCATCCCTGGCTCT CTCCTGGTACCCAGCAAGACGTCTGTTCCAGGGCAGTGTAGCATCTTTCAAGCTCCGTTACT ATGGCGATGGCCATGATGTTACAATCCCACTTGCCTGAATAATCAAGTGGGAAGGGGAAGCA GAGGGAAATGGGGCCATGTGAATGCAGCTGCTCTGTTCTCCCTACCCTGAGGAAAAACCAAA TGTTGAAGGGGCACAAGAAATGTAGCTGGAGAAGATTGATGAAAGTGCAGGTGTGTAAGGAA ATAGAACAGTCTGCTGGGAGTCAGACCTGGAATTCTGATTCCAAACTCTTTATTACTTTGGG AAGTCACTCAGCCTCCCCGTAGCCATCTCCAGGGTGACGGAACCCAGTGTATTACCTGCTGG AACCAAGGAAACTAACAATGTAGGTTACTAGTGAATACCCCAATGGTTTCTCCAATTATGCC CATGCCACCAAAACAATAAAACAAAATTCTCTAACACTGAAA

 ${\tt MWLPLGLLSLCLSPLPILSSPSLKSQACQQLLWTLPSPLVAFRANRTTYVMDVSTNQGSGME}\\ {\tt HRNHLCFCDLYDRATSPPLKCSLL}$

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امر/ امرام 5 **FIGURE 193**

GGAGCGACGTCACCGCC<u>ATG</u>GCAGGCATCAAAGCTTTGATTAGTTTGTCCTTTGGAGGAGCA ATCGGACTGATGTTTTTGATGCTTGGATGTGCCCTTCCAATATACAACAAATACTGGCCCCT CTTTGTTCTATTTTTTTACATCCTTTCACCTATTCCATACTGCATAGCAAGAAGATTAGTGG GTCGTGTCAGCTTTTGGACTCCCTATTGTATTTGCCAGAGCACATCTGATTGAGTGGGGAGC TTGTGCACTTGTTCTCACAGGAAACACAGTCATCTTTGCAACTATACTAGGCTTTTTCTTGG TCTTTGGAAGCAATGACGACTTCAGCTGGCAGCAGTGG<u>TGA</u>AAAGAAATTACTGAACTATTG TCAAATGGACTTCCTGTCATTTGTTGGCCATTCACGCACACAGGAGATGGGGCAGTTAATGC TGAATGGTATAGCAAGCCTCTTGGGGGGTATTTTAGGTGCTCCCTTCTCACTTTTATTGTAAG CATACTATTTCACAGAGACTTGCTGAAGGATTAAAAGGATTTTCTCTTTTGGAAAAGCTTG ACTGATTTCACACTTATCTATAGTATGCTTTTTTGTGGTGTCCTGCTGAATTTAAATATTTAT GTGTTTTTCCTGTTAGGTTGATTTTTTTTGGAATCAATATGCAATGTTAAACACTTTTTTAA TGTAATCATTTGCATTGGTTAGGAATTCAGAATTCCGCCGGCTCTATTACTGGTCAAGTACA TCTTTTCTCTTAAAATTATTTAGCCTCCATTATTACAAAAAATTATAAAAATTATCAG TCAGTCAGGATGACATCACTCCCAATGTTATGCAGACATACAGACGGTTGGCATACGTTATA GACTGTATACTCAGTGCAAATATAGCTGCATTTATACCTCAGAGGGGCCAAGTGTTAATGCC CATGCCCTCCGTTAAGGGTTGTTGGTTTTACTGGTAGACAGATGTTTTGTGGATTGAAAATT ATTTTATGGAATTGCTACAGAGGAGTGCTTTTCTTCTCAATTGTTAGAAGAATTTATGTTAA TAGAGTGAGTTGCAATGTGGGAAGAAATGACATTGAAATTCCAGTTTTTGAATCCTGTTTCT ATTTATAAGTGAAATTTGTGATCTCCTATCAACCTTTCATGTTTTACCCTGTTAAAATGGAC ATACATGGAACCACTACTGATGAGGGACAGTTGTATGTTTGCATCATATATGCCAGAAAACC TTCCTCTGCTTCCTCCTTTTGACTTATTTGGTATGTTGTATATATTACATAAAATAACTTTT CAAATATAGTTTAATAACACTTAGAAGTGTTTACTTACCTGGAAAATAATTGCTATGCCGTA CATTCAGAGTGCCCCCCCCCCCCCAAGGCCTTGCCATGATTAACAAGTAACTTGTTAGTCTT ACAGATAATTCATGCATTAACAGTTTAAGATTTAGACCATGGTAATAGTAGTTCTTATTCTC TAAGGTTATATCATATGTAATTTAAAAGTATTTTAAGACAAGTTTCCTGTATACCTCTGAA CTGTTTTGATTTTGAGTTCATCATGATAGATCTGCTGTTTCCTTATAAAAGGCATTTGTTGT GTGAGTTAATGCAAAGTAGCCAAGTCCAGCTATATAGCAGCTTCAGAAACATACCTGACCAA AAAATTCCCAGTAACCAGGCATGATCAATTTATAGTGGTCGTTTACATCTAATAATTATCAG GACTTTTTTCAGGAGTGGGTTATAAAAACATTCAAGTTGGTCTGACAGTATTTTGTTAAGGA TATTTGTTTGTATGTTTATTCAGTATACTTACATAAAAATTATTTCGCCATCAGCCAAAACT CAGTAATCATGACAGCTGTCTGTTGTTTTATGAAGTTTATTTCTCAAGAAAATGGGAATAAA TTTGGGATTTGTTCAGCTTTTTTACTAAAGATGCCTAAAGCCACAGGTTTTATTGCCTAACT TAAGCCATGACTTTTAGATATGAGATGACGGGAAGCAGGACGAAATATCGGCGTGTGGCTGG AGCCTTCCCACTGGAGGCTGAAAGTGGCTTGTGGTATTATAATGTTCAGATTTCAAGAGGAA GGTGCAGGTACACATGAGTTAGAGAGCTGGTGAGACAGTTGGGAACTCTTTGTGCTTGTGAT TGTCAGTGCAGTGCACTGCTACTGTTTTATCCACTTGGCCACAGACTTTTTCTAACAGCTGC GTATTATTTCTATATACTAATTGCATTGGCAGCATTGTGTCTTTGACCTTGTATACTAGCTT GACATAGTGCTGTCTCTGATTTCTAGGCTAGTTACTTGAGATATGAATTTTCCATAGAATAT GCACTGATACAACATTACCATTCTTCTATGGAAAGAAAACTTTTGATGATGAAACAATAAAG ATTTTAAATATCTATTTTAAAAAAAAAAA

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~97/310 FIGURE 194

MAGIKALISLSFGGAIGLMFLMLGCALPIYNKYWPLFVLFFYILSPIPYCIARRLVDDTDAM SNACKELAIFLTTGIVVSAFGLPIVFARAHLIEWGACALVLTGNTVIFATILGFFLVFGSND DFSWQQW

198/310

FIGURE 195A

CCCACGCGTCCGCCCACGCGTCCGCCCACGCGTCCGCCCACGCGTCCGCCC CACGCGTCCGCCCACGCGTCCGGTGCAAGCTCGCGCCGCACACTGCCTGGTGGAGGGAAGGA CCGCCCGCCCCCCAAAGCATGAGTGAGCCCGCTCTCTGCAGCTGCCCGGGGCGCGAATGG CAGGCTGTTTCCGCGGAGTAAAAGGTGGCGCCGGTCAGTGGTCGTTTCCAATGACGGACATT AACCAGACTGTCAGATCCTGGGGAGTCGCGAGCCCCGAGTTTGGAGTTTTTTCCCCCCACAA CGTCACAGTCCGAACTGCAGAGGGAAAGGAAGGCGGCAGGAAGGCGAAGCTCGGGCTCCGGC GGGCTGCCTCGGAAACACAGAGGGGTCTTCTCTCGCCCTGCATATAATTAGCCTGCACACAA AGGGAGCAGCTGAATGGAGGTTGTCACTCTCTGGAAAAGGATTTCTGACCGAGCGCTTCCAA TGGACATTCTCCAGTCTCTCTGGAAAGATTCTCGCTAATGGATTTCCTGCTGCTCGGTCTCT GTCTATACTGGCTGCTGAGGAGGCCCTCGGGGGTGGTCTTGTGTCTGCTGGGGGCCTGCTTT CAGATGCTGCCCGCCGCCCCCAGCGGGTGCCCGCAGCTGTGCCGGTGCGAGGGGCGGCTGCT GTACTGCGAGGCGCTCAACCTCACCGAGGCGCCCCACAACCTGTCCGGCCTGCTGGGCTTGT CCCTGCGCTACAACAGCCTCTCGGAGCTGCGCGCCGGCCAGTTCACGGGGTTAATGCAGCTC ACGTGGCTCTATCTGGATCACAATCACATCTGCTCCGTGCAGGGGGACGCCTTTCAGAAACT GCGCCGAGTTAAGGAACTCACGCTGAGTTCCAACCAGATCACCCAACTGCCCAACACCCCT TCCGGCCCATGCCCAACCTGCGCAGCGTGGACCTCTCGTACAACAAGCTGCAGGCGCTCGCG CCCGACCTCTTCCACGGGCTGCGGAAGCTCACCACGCTGCATATGCGGGCCAACGCCATCCA GTTTGTGCCCGTGCGCATCTTCCAGGACTGCCGCAGCCTCAAGTTTCTCGACATCGGATACA ATCAGCTCAAGAGTCTGGCGCGCAACTCTTTCGCCGGCTTGTTTAAGCTCACCGAGCTGCAC CTCGAGCACAACGACTTGGTCAAGGTGAACTTCGCCCACTTCCCGCGCCTCATCTCCCTGCA CTCGCTCTGCCTGCGGAGGAACAAGGTGGCCATTGTGGTCAGCTCGCTGGACTGGGTTTGGA ACCTGGAGAAAATGGACTTGTCGGGCAACGAGATCGAGTACATGGAGCCCCATGTGTTCGAG ACCGTGCCGCACCTGCAGTCCCTGCAGCTGGACTCCAACCGCCTCACCTACATCGAGCCCCG GATCCTCAACTCTTGGAAGTCCCTGACAAGCATCACCCTGGCCGGGAACCTGTGGGATTGCG GGCGCAACGTGTGCCCTAGCCTCGTGGCTCAGCAACTTCCAGGGGCGCTACGATGGCAAC TTGCAGTGCGCCAGCCCGGAGTACGCACAGGGCGAGGACGTCCTGGACGCCGTGTACGCCTT CCACCTGTGCGAGGATGGGGCCGAGCCCACCAGCGGCCACCTGCTCTCGGCCGTCACCAACC GCAGTGATCTGGGGCCCCCTGCCAGCTCGGCCACCACGCTCGCGGACGGCGGGGAGGGGCAG CACGACGGCACATTCGAGCCTGCCACCGTGGCTCTTCCAGGCGGCGAGCACGCCGAGAACGC CGTGCAGATCCACAAGGTGGTCACGGGCACCATGGCCCTCATCTTCTCCTCATCGTGG TTTGTCACGCAGCGCAGGAAGCAAAAGCAGAAAAGACCATGCATCAGATGGCTGCCATGTC TGCCCAGGAATACTACGTTGATTACAAACCGAACCACATTGAGGGAGCCCTGGTGATCATCA ACGAGTATGGCTCGTGTACCTGCCACCAGCAGCCCGCGAGGGAATGCGAGGTG<u>TGA</u>TTGTCC CCAGGCTGGGGTCTCCTTGTCTGTGCTCTGATATGCTCCTTGACTGAAACTTTAAGGGGATC TCTCCCAGAGACTTGACATTTTAGCTTTATTGTGTCTTAAAAAACAAAAGCGAATTAAAAACAC AACAAAAAACCCCACCCCACAACCTTCAGGACAGTCTATCTTAAATTTCATATGAGAACTCC TTCCTCCCTTTGAAGATCTGTCCATATTCAGGAATCTGAGAGTGTAAAAAAAGGTGGCCATAA GACAGAGAGAGAATAATCGTGCTTTGTTTTATGCTACTCCTCCCACCCTGCCCATGATTAAA CATCATGTATGTAGAAGATCTTAAGTCCATACGCATTTCATGAAGAACCATTGGAAAGAGGA ATCTGCAATCTGGGAGCTTAAGAGCAAATGATGACCATAGAAAGCTATGTTCTTACTTTGTG CGGGAATTTAGCTCACATCATTTCATGCCCCTGTGCCTCTAGCTCTGGAGATTGGTGGGGGG AGGTGGGGGGAAACGGCAGGAATAAGGGAAAGTGGTAGTTTTAACTAAGGTTTTGTAACACT TGAAATCTTTTCTCTCAAATTAATTATCTTTAAGCTTCAAGAAACTTGCTCTGACCCCTC TATTCTTCCCACAGAGGGTGCTAATCTCATTATGCTGTGCTATCTGAAAAGAACTTAAGGCC ACAATTCACGTCTCGTCCTGGGCATTGTGATGGATTGACCCTCCATTTGCAGTACCTTCCCA GCTGATTAAAGTTCAGCAGTGGTATTGAGGTTTTTCGAATATTTATATAGAAAAAAAGTCTT TTCACATGACAAATGACACTCTCACACCAGTCTTAGCCCTAGTAGTTTTTTAGGTTGGACCA GAGGAAGCAGGTTAAATGAGACCTGTCCTCTGCTGCACTCAGAAAAAATAGGCAGTCCCTGA TGCTCAGATCTTAGCCTTGATATTAATAGTTGAGACCACCTACCCACAATGCAGCCTATACT CCCAAGACTACAAAGTTACCATCGCAAAGGAAAGGTTATTCCAGTAAAAGGAAATAGTTTTC TCAACCATTTAAAAATATTCTTCTGAACTCATCAAAGTAGAAGAGCCCCCAACCTTTTCTCT CTGCCTTCAAGAAGGCAGACATTTGGTATGATTTAGCATCAACAACACATTTATGAGTATAT

FIGURE 195B

200/310 FIGURE 196

MDFLLIGLCLYWLLRRPSGVVLCLIGACFQMLPAAPSGCPQLCRCEGRLLYCEALNLTEAPH
NLSGLIGLSLRYNSLSELRAGQFTGLMQLTWLYLDHNHICSVQGDAFQKLRRVKELTLSSNQ
ITQLPNTTFRPMPNLRSVDLSYNKLQALAPDLFHGLRKLTTLHMRANAIQFVPVRIFQDCRS
LKFLDIGYNQLKSLARNSFAGLFKLTELHLEHNDLVKVNFAHFPRLISLHSLCLRRNKVAIV
VSSLDWVWNLEKMDLSGNEIEYMEPHVFETVPHLQSLQLDSNRLTYIEPRILNSWKSLTSIT
LAGNLWDCGRNVCALASWLSNFQGRYDGNLQCASPEYAQGEDVLDAVYAFHLCEDGAEPTSG
HLLSAVTNRSDLGPPASSATTLADGGEGQHDGTFEPATVALPGGEHAENAVQIHKVVTGTMA
LIFSFLIVVLVLYVSWKCFPASLRQLRQCFVTQRRKQKQKQTMHQMAAMSAQEYYVDYKPNH
IEGALVIINEYGSCTCHQQPARECEV

-e01/310 FIGURE 197

MGVLGRVLLWLQLCALTQAVSKLWVPNTDFDVAANWSQNRTPCAGGAVEFPADKMVSVLVQE GHAVSDMLLPLDGELVLASGAGFGVSDVGSHLDCGAGEPAVFRDSDRFSWHDPHLWRSGDEA PGLFFVDAERVPCRHDDVFFPPSASFRVGLGPGASPVRVRSISALGRTFTRDEDLAVFLASR AGRLRFHGPGALSVGPEDCADPSGCVCGNAEAQPWICAALLQP

MGPVKQLKRMFEPTRLIATIMVLLCFALTLCSAFWWHNKGLALIFCILQSLALTWYSLSFIP FARDAVKKCFAVCLA

205/310

FIGURE 201

TTGAGCGCAGGTGAGCTCCTGCGCGTTCCGGGGGCGTTCCTCCAGTCACCCTCCCGCCGTTA ACTACCATCCATAGCCAGATAGATTATCTTACACTGAACTGATCAAGTACTTTGAAAAATGAC TTCGAAATTTATCTTGGTGTCCTTCATACTTGCTGCACTGAGTCTTTCAACCACCTTTTCTC TCCAACTAGACCAGCAAAAGGTTCTACTAGTTTCTTTTGATGGATTCCGTTGGGATTACTTA TATAAAGTTCCAACGCCCCATTTTCATTATATTATGAAATATGGTGTTCACGTGAAGCAAGT TACTAATGTTTTTATTACAAAAACCTACCCTAACCATTATACTTTGGTAACTGGCCTCTTTG CAGAGAATCATGGGATTGTTGCAAATGATATGTTTGATCCTATTCGGAACAAATCTTTCTCC TTGGATCACATGAATATTTATGATTCCAAGTTTTGGGAAGAAGCGACACCAATATGGATCAC AAACCAGAGGGCAGGACATACTAGTGGTGCAGCCATGTGGCCCGGAACAGATGTAAAAATAC ATAAGCGCTTTCCTACTCATTACATGCCTTACAATGAGTCAGTTTCATTTGAAGATAGAGTT GCCAAAATTGTTGAATGGTTTACGTCAAAAGAGCCCATAAATCTTGGTCTTCTCTATTGGGA AGACCCTGATGACATGGGCCACCATTTGGGACCTGACAGTCCGCTCATGGGGCCTGTCATTT CAGATATTGACAAGAAGTTAGGATATCTCATACAAATGCTGAAAAAGGCAAAGTTGTGGAAC ACTCTGAACCTAATCATCACAAGTGATCATGGAATGACGCAGTGCTCTGAGGAAAGGTTAAT CCATCTTGCCAAAAGAAGGTAAATTTGATGAAGTCTATGAAGCACTAACTCACGCTCATCCT AATCTTACTGTTTACAAAAAAGAAGACGTTCCAGAAAGGTGGCATTACAAATACAACAGTCG **AATTCAACCAATCATAGCAGTGGCTGATGAAGGGTGGCACATTTTACAGAATAAGTCAGATG** ACTTTCTGTTAGGCAACCACGGTTACGATAATGCGTTAGCAGATATGCATCCAATATTTTTA GCCCATGGTCCTGCCTTCAGAAAGAATTTCTCAAAAGAAGCCATGAACTCCACAGATTTGTA CCCACTACTATGCCACCTCCTCAATATCACTGCCATGCCACACAATGGATCATTCTGGAATG TCCAGGATCTGCTCAATTCAGCAATGCCAAGGGTGGTCCCTTATACACAGAGTACTATACTC CTCCCTGGTAGTGTTAAACCAGCAGAATATGACCAAGAGGGGTCATACCCTTATTTCATAGG GGTCTCTCTTGGCAGCATTATAGTGATTGTATTTTTTGTAATTTTCATTAAGCATTTAATTC ACAGTCAAATACCTGCCTTACAAGATATGCATGCTGAAATAGCTCAACCATTATTACAAGCC TAATGTTACTTTGAAGTGGATTTGCATATTGAAGTGGAGATTCCATAATTATGTCAGTGTTT AAAGGTTTCAAATTCTGGGAAACCAGTTCCAAACATCTGCAGAAACCATTAAGCAGTTACAT AGATCCTGCTTTATTTGGACTTGGCGCAGATAATGTATATTTTAGCAACTTTGCACTATGT AAAGTACCTTATATATTGCACTTTAAATTTCTCTCCTGATGGGTACTTTAATTTGAAATGCA CTTTATGGACAGTTATGTCTTATAACTTGATTGAAAATGACAACTTTTTGCACCCATGTCAC AGAATACTTGTTACGCATTGTTCAAACTGAAGGAAATTTCTAATAATCCCGAATAATGAACA TAGAAATCTATCTCCATAAATTGAGAGAAGAAGAAGGTGATAAGTGTTGAAAATTAAATGTG ATAACCTTTGAACCTTGAATTTTGGAGATGTATTCCCAACAGCAGAATGCAACTGTGGGCAT AAATACTGACAGATTCGTTCTAAATATATTGTTTCTGTCATAAAATTATTGTGATTTCCTGA TGAGTCATATTACTGTGATTTTCATAATAATGAAGACACCATGAATATACTTTTCTTATA TAGTTCAGCAATGGCCTGAATAGAAGCAACCAGGCACCATCTCAGCAATGTTTTCTCTFGTT **АААААААААААА**

€06/310 FIGURE 202

MTSKFILVSFILAALSLSTTFSLQLDQQKVLLVSFDGFRWDYLYKVPTPHFHYIMKYGVHVK
QVTNVFITKTYPNHYTLVTGLFAENHGIVANDMFDPIRNKSFSLDHMNIYDSKFWEEATPIW
ITNQRAGHTSGAAMWPGTDVKIHKRFPTHYMPYNESVSFEDRVAKIVEWFTSKEPINLGLLY
WEDPDDMGHHLGPDSPLMGPVISDIDKKLGYLIQMLKKAKLWNTLNLIITSDHGMTQCSEER
LIELDQYLDKDHYTLIDQSPVAAILPKEGKFDEVYEALTHAHPNLTVYKKEDVPERWHYKYN
SRIQPIIAVADEGWHILQNKSDDFLLGNHGYDNALADMHPIFLAHGPAFRKNFSKEAMNSTD
LYPLLCHLLNITAMPHNGSFWNVQDLLNSAMPRVVPYTQSTILLPGSVKPAEYDQEGSYPYF
IGVSLGSIIVIVFFVIFIKHLIHSQIPALQDMHAEIAQPLLQA

حوم / المارة FIGURE 203

GGATTTTTGTGATCCGCGATTCGCTCCCACGGGCGGACCTTTGTAACTGCGGGAGGCCCAG AGAGAGGCCAAGCCCTTGCCTTGGGTCACACAGCCAAAGGAGGCAGAGCCAGAACTCACAA CCAGATCCAGAGGCAACAGGGAC<u>ATG</u>GCCACCTGGGACGAAAAGGCAGTCACCCGCAGGGCC AAGGTGGCTCCCGCTGAGAGGATGAGCAAGTTCTTAAGGCACTTCACGGTCGTGGGAGACGA AGCAGCCACCACACCAGTCTCAGGCGAGGAAGGCAGAGCTGCAGCCCCTGACGTTGCC CCTGCCCCTGGCCCCGCACCCAGGGCCCCCCTTGACTTCAGGGGCATGTTGAGGAAACTGTT CAGCTCCCACAGGTTTCAGGTCATCATCTGCTTGGTGGTTCTGGATGCCCTCCTGGTGC TTGCTGAGCTCATCCTGGACCTGAAGATCATCCAGCCCGACAAGAATAACTATGCTGCCATG GTATTCCACTACATGAGCATCACCATCTTGGTCTTTTTTATGATGGAGATCATCTTTAAATT ATTTGTCTTCCGCCTGAGTTCTTTCACCACAAGTTTGAGATCCTGGATGCCCGTCGTGGTGG TGGTCTCATTCATCCTGGACATTGTCCTCCTGTTCCAGGAGCACCAGTTTGAGGCTCTGGGC CTGCTGATTCTGCTCCGGCTGTGGCCGGGTGGCCCGGATCATCAATGGGATTATCATCTCAGT TAAGACACGTTCAGAACGGCAACTCTTAAGGTTAAAACAGATGAATGTACAATTGGCCGCCA ${\tt AGATTCAACACCTTGAGTTCAGCTGCTCTGAGAAGCCCCTGGAC\underline{{\tt TGA}}{\tt TGAGTTTGCTGTATC}}$ AACCTGTAAGGAGAAGCTCTCTCCGGATGGCTATGGGAATGAAAGAATCCGACTTCTACTCT CAGGCTGGCATGTTCACTGGGCTGGTGTTACGACAGAGAACCTGACAGTCACTGGCCAGTTA TCACTTCAGATTACAAATCACACAGAGCATCTGCCTGTTTTCAATCACAAGAGAACAAAACC AAAATCTATAAAGATATTCTGAAAATATGACAGAATTTGACAAATAAAAGCATAAACGTGTA ААААААААААААААААААААААААААААААА

८०४/७।० FIGURE 204

MATWDEKAVTRRAKVAPAERMSKFLRHFTVVGDDYHAWNINYKKWENEEEEEEEQPPPTPV
SGEEGRAAAPDVAPAPGPAPRAPLDFRGMLRKLFSSHRFQVIIICLVVLDALLVLAELILDL
KIIQPDKNNYAAMVFHYMSITILVFFMMEIIFKLFVFRLSSFTTSLRSWMPVVVVVSFILDI
VLLFQEHQFEALGLLILLRLWRVARIINGIIISVKTRSERQLLRLKQMNVQLAAKIQHLEFS
CSEKPLD

-२०५ /३।० FIGURE 205

CGGCTCGAGCTCGAGCCGAATCGGCTCGAGGGGCAGTGGAGCACCCAGCAGCAGCCCCAAC<u>AT</u> **GCTCTGTCTGTGCCTGTACGTGCCGGTCATCGGGGAAGCCCAGACCGAGTTCCAGTACTTTG** AGTCGAAGGGGCTCCCTGCCGAGCTGAAGTCCATTTTCAAGCTCAGTGTCTTCATCCCCTCC CAGGAATTCTCCACCTACCGCCAGTGGAAGCAGAAAATTGTACAAGCTGGAGATAAGGACCT TGATGGGCAGCTAGACTTTGAAGAATTTGTCCATTATCTCCAAGATCATGAGAAGAAGCTGA GGCTGGTGTTTAAGATTTTGGACAAAAAGAATGATGGACGCATTGACGCGCAGGAGATCATG CATGGATAAAAACGGCACGATGACCATCGACTGGAACGAGTGGAGAGACTACCACCTCCTCC ACCCCGTGGAAAACATCCCCGAGATCATCCTCTACTGGAAGCATTCCACGATCTTTGATGTG GGTGAGAATCTAACGGTCCCGGATGAGTTCACAGTGGAGGAGAGGCAGACGGGGATGTGGTG GAGACACCTGGTGGCAGGAGGTGGGGCAGGGGCCGTATCCAGAACCTGCACGGCCCCCTGG ACAGGCTCAAGGTGCTCATGCAGGTCCATGCCTCCCGCAGCAACAACATGGGCATCGTTGGT GGCTTCACTCAGATGATTCGAGAAGGAGGGGCCAGGTCACTCTGGCGGGGCAATGGCATCAA CGTCCTCAAAATTGCCCCCGAATCAGCCATCAAATTCATGGCCTATGAGCAGATCAAGCGCC TTGTTGGTAGTGACCAGGAGACTCTGAGGATTCACGAGAGGCTTGTGGCAGGGTCCTTGGCA GGGGCCATCGCCCAGAGCAGCATCTACCCAATGGAGGTCCTGAAGACCCGGATGGCGCTGCG GAAGACAGGCCAGTACTCAGGAATGCTGGACTGCGCCAGGAGGATCCTGGCCAGAGAGGGGG TGGCCGCCTTCTACAAAGGCTATGTCCCCAACATGCTGGGCATCATCCCCTATGCCGGCATC GACCTTGCAGTCTACGAGACGCTCAAGAATGCCTGGCTGCAGCACTATGCAGTGAACAGCGC GGACCCCGGCGTGTTTGTGCTCCTGGCCTGTGGCACCATGTCCAGTACCTGTGGCCAGCTGG CCAGCTACCCCTGGCCCTAGTCAGGACCCGGATGCAGGCGCAAGCCTCTATTGAGGGCGCT CCGGAGGTGACCATGAGCAGCCTCTTCAAACATATCCTGCGGACCGAGGGGGCCTTCGGGCT GTACAGGGGGCTGGCCCCCAACTTCATGAAGGTCATCCCAGCTGTGAGCATCAGCTACGTGG TCTACGAGAACCTGAAGATCACCCTGGGCGTGCAGTCGCGG<u>TGA</u>CGGGGGGAGGGCCCCCG GCAGTGGACTCGCTGATCCTGGGCCGCAGCCTGGGGTGTGCAGCCATCTCATTCTGTGAATG GGGGAGAGCTGGCAGGCCCAGGGCTTGTCCTGCTGACCCCAGCAGACCCTCCTGTTGGTTCC AGCGAAGACCACAGGCATTCCTTAGGGTCCAGGGTCAGCAGGCTCCGGGCTCACATGTGTAA GGACAGGACATTTTCTGCAGTGCCTGCCAATAGTGAGCTTGGAGCCTGGAGGCCGGCTTAGT TCTTCCATTTCACCCTTGCAGCCAGCTGTTGGCCACGGCCCCTGCCCTCTGGTCTGCCGTGC ATCTCCCTGTGCCCTCTTGCTGCCTGCCTGTCTGAGGTAAGGTGGGAGGAGGCTACAG CCCACATCCCACCCCTCGTCCAATCCCATAATCCATGATGAAAGGTGAGGTCACGTGGCCT GATCTGGCCTTGTGGTCACTGGCATCTGAGCCCTGCTGATGGCTGGGGCTCTCGGGCATGCT TGGGAGTGCAGGGGGCTCGGCTGGCCTGGCTGCACAGAAGGCAAGTGCTGGGGCTCA TGGTGCTCTGAGCTGGCCTGGACCCTGTCAGGATGGGCCCCACCTCAGAACCAAACTCACTG TCCCCACTGTGGCATGAGGGCAGTGGAGCACCATGTTTGAGGGCGAAGGGCAGAGCGTTTGT GTGTTCTGGGGAGGAAAAGGTGTTGGAGGCCTTAATTATGGACTGTTGGGAAAAGGG TTTTGTCCAGAAGGACAAGCCGGACAAATGAGCGACTTCTGTGCTTCCAGAGGAAGACGAGG GAGCAGGAGCTTGGCTGACTGCTCAGAGTCTGTTCTGACGCCCTGGGGGTTCCTGTCCAACC CCAGCAGGGGCGCAGCGGGACCAGCCCCACATTCCACTTGTGTCACTGCTTGGAACCTATTT GCTTGTCATTTTCAAGTTCATTTTTTATTCATATTTATGTTCATGGTTGATTGTACCTTCCC AAGCCCGCCCAGTGGGATGGGAGGAGGAGGAGAAGGGGGGCCTTGGGCCGCTGCAGTCACAT CTGTCCAGAGAAATTCCTTTTGGGACTGGAGGCAGAAAAGCGGCCAGAAGGCAGCAGCCCTG GCTCCTTTCCTTTGGCAGGTTGGGGAAGGGCTTGCCCCCAGCCTTAGGATTTCAGGGTTTGA CTGGGGGCGTGGAGAGAGGGAGGAACCTCAATAACCTTGAAGGTGGAATCCAGTTATTTC CTGCGCTGCGAGGGTTTCTTTATTTCACTCTTTTCTGAATGTCAAGGCAGTGAGGTGCCTCT CAGCCTTCTGCTGCCTTAACAATGCCGGCCAACTGGCGACCTCACGGTTGCACTTCC ATTCCACCAGAATGACCTGATGAGGAAATCTTCAATAGGATGCAAAGATCAATGCAAAAATT

-ep /310

FIGURE 206

MLCLCLYVPVIGEAQTEFQYFESKGLPAELKSIFKLSVFIPSQEFSTYRQWKQKIVQAGDKD
LDGQLDFEEFVHYLQDHEKKLRLVFKILDKKNDGRIDAQEIMQSLRDLGVKISEQQAEKILK
SMDKNGTMTIDWNEWRDYHLLHPVENIPEIILYWKHSTIFDVGENLTVPDEFTVEERQTGMW
WRHLVAGGGAGAVSRTCTAPLDRLKVLMQVHASRSNNMGIVGGFTQMIREGGARSLWRGNGI
NVLKIAPESAIKFMAYEQIKRLVGSDQETLRIHERLVAGSLAGAIAQSSIYPMEVLKTRMAL
RKTGQYSGMLDCARRILAREGVAAFYKGYVPNMLGIIPYAGIDLAVYETLKNAWLQHYAVNS
ADPGVFVLLACGTMSSTCGQLASYPLALVRTRMQAQASIEGAPEVTMSSLFKHILRTEGAFG
LYRGLAPNFMKVIPAVSISYVVYENLKITLGVQSR

GGAAGGCAGCGCAGCTCCACTCAGCCAGTACCCAGATACGCTGGGAACCTTCCCCAGCCAT CAATTGCACTCATCATTGGCTTTTGGTATTTCAGGGAGACACTCCATCACAGTCACTACTGTC GCCTCAGCTGGGAACATTGGGGAGGATGGAATCCTGAGCTGCACTTTTGAACCTGACATCAA ACTTTCTGATATCGTGATACAATGGCTGAAGGAAGGTGTTTTAGGCTTGGTCCATGAGTTCA AAGAAGGCAAAGATGAGCTGTCGGAGCAGGATGAAATGTTCAGAGGCCGGACAGCAGTGTTT GCTGATCAAGTGATAGTTGGCAATGCCTCTTTGCGGCTGAAAAACGTGCAACTCACAGATGC TGGCACCTACAAATGTTATATCATCACTTCTAAAGGCAAGGGGAATGCTAACCTTGAGTATA AAACTGGAGCCTTCAGCATGCCGGAAGTGAATGTGGACTATAATGCCAGCTCAGAGACCTTG CGGTGTGAGGCTCCCCGATGGTTCCCCCAGCCCACAGTGGTCTGGGCATCCCAAGTTGACCA GGGAGCCAACTTCTCGGAAGTCTCCAATACCAGCTTTGAGCTGAACTCTGAGAATGTGACCA TGAAGGTTGTGTCTGTGCTCTACAATGTTACGATCAACACACATACTCCTGTATGATTGAA AATGACATTGCCAAAGCAACAGGGGATATCAAAGTGACAGAATCGGAGATCAAAAGGCGGAG GGGCACTTCTGCCTCTCAGCCCTTACCTGATGCTAAAA<u>TAA</u>TGTGCCTTGGCCACAAAAAG CATGCAAAGTCATTGTTACAACAGGGATCTACAGAACTATTTCACCACCAGATATGACCTAG TTTTATATTTCTGGGAGGAAATGAATTCATATCTAGAAGTCTGGAGTGAGCAAACAAGAGCA GACATATTAGAAGTTGGGAAAATAATTCATGTGAACTAGACAAGTGTGTTAAGAGTGATAAG GGGGAGTGAGAGGACAGGATAGTGCATGTTCTTTGTCTCTGAATTTTTAGTTATATGTGCTG TAATGTTGCTCTGAGGAAGCCCCTGGAAAGTCTATCCCAACATATCCACATCTTATATTCCA CAAATTAAGCTGTAGTATGTACCCTAAGACGCTGCTAATTGACTGCCACTTCGCAACTCAGG GGCGGCTGCATTTTAGTAATGGGTCAAATGATTCACTTTTTATGATGCTTCCAAAGGTGCCT TGGCTTCTCTCCCAACTGACAAATGCCAAAGTTGAGAAAAATGATCATAATTTTAGCATAA ACAGAGCAGTCGGGGACACCGATTTTATAAATAAACTGAGCACCTTCTTTTTAAACAAAAAA

~12/310 FIGURE 208

MASLGQILFWSIISIIIILAGAIALIIGFGISGRHSITVTTVASAGNIGEDGILSCTFEPDI KLSDIVIQWLKEGVLGLVHEFKEGKDELSEQDEMFRGRTAVFADQVIVGNASLRLKNVQLTD AGTYKCYIITSKGKGNANLEYKTGAFSMPEVNVDYNASSETLRCEAPRWFPQPTVVWASQVD QGANFSEVSNTSFELNSENVTMKVVSVLYNVTINNTYSCMIENDIAKATGDIKVTESEIKRR SHLQLLNSKASLCVSSFFAISWALLPLSPYLMLK

~13/310

FIGURE 209

GAATTTGTAGAAGACAGCGGCGTTGCCATGGCGGCGTCTCTGGGGCAGGTGTTGGCTCTGGT GCTGGTGGCCGCTCTGTGGGGTGGCACGCAGCCGCTGCTGAAGCGGGCCTCCGCCGGCCTGC AGCGGGTTCATGAGCCGACCTGGGCCCAGCAGTTGCTACAGGAGATGAAGACCCTCTTCTTG AATACTGAGTACCTGATGCCCTTTCTCCTCAACCAGTGTGGATCCCTTCTCTATTACCTCAC CTTGGCATCGACAGATCTGACCCTGGCTGTGCCCATCTGTAACTCTCTGGCTATCATCTTCA CACTGATTGTTGGGAAGGCCCTTGGAGAAGATATTGGTGGAAAACGTAAGTTAGACTACTGC CTCCCCAGAGTGGGTGAGGACACGGCCTTTTCCCATCCTGCCCCTTTCCTCTGCAGCTGTTTT GCTTCCTTGTGGCCATCAGAGTTCCCTTCCCCTGGACAGTCTGGAGAAAGACAGAGGCTGGG GTTTGGGAT<u>TGA</u>AGACCAGACCCCATCTGAGCCCTTCCTCCAGCCCTGTACCAGCTCCTACT GGCATGGCTGAGCTCAGACCCTCCTGATTTCTGCCTATTATCCCAGGAGCAGTTGCTGGCAT GGTGCTCACCGTGATAGGAATTTCACTCTGCATCACAAGCTCAGTGAGTAAGACCCAGGGGC AACAGTCTACCCTTTGAGTGGGCCGAACCCACTTCCAGCTCTGCTGCCTCCAGGAAGCCCCT GGGCCATGAAGTGCTGGCAGTGAGCGGATGGACCTAGCACTTCCCCTCTCTGGCCTTAGCTT CCTCCTCTCTTATGGGGATAACAGCTACCTCATGGATCACAATAAGAGAACAAGAGTGAAAG AGTTTTGTAACCTTCAAGTGCTGTTCAGCTGCGGGGATTTAGCACAGGAGACTCTACGCTCA CCCTCAGCAACCTTTCTGCCCCAGCAGCTCTCTTCCTGCTAACATCTCAGGCTCCCAGCCCA GCCACCATTACTGTGGCCTGATCTGGACTATCATGGTGGCAGGTTCCATGGACTGCAGAACT CCAGCTGCATGGAAAGGGCCAGCTGCAGACTTTGAGCCAGAAATGCAAACGGGAGGCCTCTG GGACTCAGTCAGAGCGCTTTGGCTGAATGAGGGGTGGAACCGAGGGAAGAAGGTGCGTCGGA AAATCCTCACTGCCAGCCCCTCTTAAACAGGTAGAGAGCTGTGAGCCCCAGCCCAGCCTGAC

214/310

FIGURE 210

MAASLGQVLALVLVAALWGGTQPLLKRASAGLQRVHEPTWAQQLLQEMKTLFLNTEYLMPFL LNQCGSLLYYLTLASTDLTLAVPICNSLAIIFTLIVGKALGEDIGGKRKLDYCECGTQLCGS RHTCVSSFPEPISPEWVRTRPFPILPFPLQLFCFLVAIRVPFPWTVWRKTEAGVWD

حم5/310 FIGURE 211

CTTCTGTAGGACAGTCACCAGGCCAGATCCAGAAGCCTCTCTAGGCTCCAGCTTTCTCTGTG GAAGATGACAGCAATTATAGCAGGACCCTGCCAGGCTGTCGAAAAGATTCCGCAATAAAACT TTGCCAGTGGGAAGTACCTAGTGAAACGGCCTAAGATGCCACTTCTTCTCATGTCCCAGGCT TGAGGCCCTGTGGTCCCCATCCTTGGGAGAAGTCAGCTCCAGCACCATGAAGGGCATCCTCG TTGCTGGTATCACTGCAGTGCTTGTTGCAGCTGTAGAATCTCTGAGCTGCGTGCAGTGTAAT TCATGGGAAAAATCCTGTGTCAACAGCATTGCCTCTGAATGTCCCTCACATGCCAACACCAG CTGTATCAGCTCCTCAGCCAGCTCCTCTCTAGAGACACCAGTCAGATTATACCAGAATATGT TCTGCTCAGCGGAGAACTGCAGTGAGGAGACACACATTACAGCCTTCACTGTCCACGTGTCT GCTGAAGAACACTTTCATTTTGTAAGCCAGTGCTGCCAAGGAAAGGAATGCAGCAACACCAG CGATGCCCTGGACCCTCCCCTGAAGAACGTGTCCAGCAACGCAGAGTGCCCTGCTTGTTATG AATCTAATGGAACTTCCTGTCGTGGGAAGCCCTGGAAATGCTATGAAGAAGAACAGTGTGTC TTTCTAGTTGCAGAACTTAAGAATGACATTGAGTCTAAGAGTCTCGTGCTGAAAGGCTGTTC CAACGTCAGTAACGCCACCTGTCAGTTCCTGTCTGGTGAAAACAAGACTCTTGGAGGAGTCA TCCCACACGTGGGCTCCAAAGCTTCCCTCTACCTCTTGGCCCTTGCCAGCCTCCTTCTTCG GGGACTGCTGCCCTGAGGTCCTGGGGCTGCACTTTGCCCAGCACCCCATTTCTGCTTCTCTG AGGTCCAGAGCACCCCTGCGGTGCTGACACCCTCTTTCCCTGCTCTGCCCCGTTTAACTGC CCAGTAAGTGGGAGTCACAGGTCTCCAGGCAATGCCGACAGCTGCCTTGTTCTTCATTATTA

215/310

FIGURE 212

MKGILVAGITAVLVAAVESLSCVQCNSWEKSCVNSIASECPSHANTSCISSSASSSLETPVR LYQNMFCSAENCSEETHITAFTVHVSAEEHFHFVSQCCQGKECSNTSDALDPPLKNVSSNAE CPACYESNGTSCRGKPWKCYEEEQCVFLVAELKNDIESKSLVLKGCSNVSNATCQFLSGENK TLGGVIFRKFECANVNSLTPTSAPTTSHNVGSKASLYLLALASLLLRGLLP

جمع/310 FIGURE 213

GGCCTCGGTTCAAACGACCCGGTGGGTCTACAGCGGAAGGGAGCGAAGGTAGGAGGCA GGGCTTGCCTCACTGGCCACCCTCCCAACCCCAAGAGCCCAGCCCCATGGTCCCCGCCGCCG ACCCAGACTCCGACCGAAATGCAGCGGGTCAGTTTACGCTTTGGGGGCCCCCATGACCCGCAG CTACCGGAGCACCGCCCGGACTGGTCTTCCCCGGAAGACAAGGATAATCCTAGAGGACGAGA ATGATGCCATGGCCGACGCCGACCGCCTGGCTGGACCAGCGCTGCCGAGCTCTTGGCCGCC ACGGTGTCCACCGGCTTTAGCCGGTCGTCCGCCATTAACGAGGAGGATGGGTCTTCAGAAGA GGGGGTTGTGATTAATGCCGGAAAGGATAGCACCAGCAGAGAGCTTCCCAGTGCGACTCCCA ATACAGCGGGGAGTTCCAGCACGAGGTTTATAGCCAATAGTCAGGAGCCTGAAATCAGGCTG ACTTCAAGCCTGCCGCGCTCCCCCGGGAGGTCTACTGAGGACCTGCCAGGCTCGCAGGCCAC CCTGAGCCAGTGGTCCACACCTGGGTCTACCCCGAGCCGGTGGCCGTCACCCTCACCCACAG CCATGCCATCTCCTGAGGATCTGCGGCTGGTGCTGATGCCCTGGGGCCCGTGGCACTGCCAC TGCAAGTCGGGCACCATGAGCCGGAGCCGGTCTGGGAAGCTGCACGGCCTTTCCGGGCGCCT TCGAGTTGGGGCGCTGAGCCAGCTCCGCACGGAGCACAAGCCTTGCACCTATCAACAATGTC CCTGCAACCGACTTCGGGAAGAGTGCCCCCTGGACAAGTCTCTGTACTGACACCAACTGT GCCTCTCAGAGCACCACCAGTACCAGGACCACCACTACCCCCTTCCCCACCATCCACCTCAG AAGCAGTCCCAGCCTGCCACCCGCCAGCCCTGCCCAGCCTTTTTTGGAAACGGTCA GGATTGGCCTGGAGGATATTTGGAATAGCCTCTCTTCAGTGTTCACAGAGATGCAACCAATA GACAGAAACCAGAGGTAATGGCCACTTCATCCACATGAGGAGATGTCAGTATCTCAACCTCT CTTGCCCTTTCAATCCTAGCACCCACTAGATATTTTTAGTACAGAAAAACAAAACTGGAAAA CACAA

e-18/310

FIGURE 214

MVPAAGALLWVLLLNLGPRAAGAQGLTQTPTEMQRVSLRFGGPMTRSYRSTARTGLPRKTRI
ILEDENDAMADADRLAGPAAAELLAATVSTGFSRSSAINEEDGSSEEGVVINAGKDSTSREL
PSATPNTAGSSSTRFIANSQEPEIRLTSSLPRSPGRSTEDLPGSQATLSQWSTPGSTPSRWP
SPSPTAMPSPEDLRLVLMPWGPWHCHCKSGTMSRSRSGKLHGLSGRLRVGALSQLRTEHKPC
TYQQCPCNRLREECPLDTSLCTDTNCASQSTTSTRTTTTPFPTIHLRSSPSLPPASPCPALA
FWKRVRIGLEDIWNSLSSVFTEMQPIDRNQR

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CCCGGGTCGACCCACGCGTCCGGGGAGAAAGG<u>ATG</u>GCCGGCCTGGCGGCGCGGTTGGTCCTG CTAGCTGGGGCAGCGCCGCTGGCGAGCGGCTCCCAGGGCGACCGTGAGCCGGTGTACCGCGA CTGCGTACTGCAGTGCGAAGAGCAGAACTGCTCTGGGGGGCGCTCTGAATCACTTCCGCTCCC GCCAGCCAATCTACATGAGTCTAGCAGGCTGGACCTGTCGGGACGACTGTAAGTATGAGTGT ATGTGGGTCACCGTTGGGCTCTACCTCCAGGAAGGTCACAAAGTGCCTCAGTTCCATGGCAA GTGGCCCTTCTCCCGGTTCCTGTTCTTTCAAGAGCCGGCATCGGCCGTGGCCTCGTTTCTCA ATGGCCTGGCCAGCCTGGTGATGCTCTGCCGCTACCGCACCTTCGTGCCAGCCTCCTCCCCC **ATGTACCACACCTGTGTGGCCTTCGCCTGGGTGTCCCTCAATGCATGGTTCTGGTCCACAGT** CTTCCACACCAGGGACACTGACCTCACAGAGAAAATGGACTACTTCTGTGCCTCCACTGTCA TCCTACACTCAATCTACCTGTGCTGCGTCAGGACCGTGGGGCTGCAGCACCCAGCTGTGGTC AGTGCCTTCCGGGCTCTCCTGCTGCTCATGCTGACCGTGCACGTCTCCTACCTGAGCCTCAT CCGCTTCGACTATGGCTACAACCTGGTGGCCAACGTGGCTATTGGCCTGGTCAACGTGGTGT **GGTGGCTGGCCTGGTGCAACCAGCGGCGCTGCCTCACGTGCGCAAGTGCGTGGTG** GTGGTCTTGCTGCAGGGGCTGTCCCTGCTCGAGCTGCTTGACTTCCCACCGCTCTTCTG GGTCCTGGATGCCATGCCATCTGGCACATCAGCACCATCCCTGTCCACGTCCTCTTTTTCA GCTTTCTGGAAGATGACAGCCTGTACCTGCTGAAGGAATCAGAGGACAAGTTCAAGCTGGAC TGAAGACCTTGGAGCGAGTCTGCCCCAGTGGGGATCCTGCCCCCGCCCTGCTGGCCTCCCTT CTCCCTCAACCCTTGAGATGATTTTCTCTTTTCAACTTCTTGAACTTGGACATGAAGGATG TGGGCCCAGAATCATGTGGCCAGCCCACCCCTGTTGGCCCTCACCAGCCTTGGAGTCTGTT CTAGGGAAGGCCTCCCAGCATCTGGGACTCGAGAGTGGGCAGCCCCTCTACCTCCTGGAGCT GAACTGGGGTGGAACTGAGTGTGTTCTTAGCTCTACCGGGAGGACAGCTGCCTGTTTCCTCC CCACCAGCCTCCCCCACATCCCCAGCTGCCTGGCTGGGTCCTGAAGCCCTCTGTCTACCT GGGAGACCAGGGACCACAGGCCTTAGGGATACAGGGGGTCCCCTTCTGTTACCACCCCCAC GCGATTCTCCCCATGGGATCTTGAGGGACCAAGCTGCTGGGATTGGGAAGGAGTTTCACCCT GACCGTTGCCCTAGCCAGGTTCCCAGGAGGCCTCACCATACTCCCTTTCAGGGCCAGGGCTC CAGCAAGCCCAGGGCAAGGATCCTGTGCTGCTGTCTGGTTGAGAGCCTGCCACCGTGTGTCG GAGCTCAGGCCTAGGTGCGCAGTGTGGAGACGGGTGTTGTCGGGGAAGAGGTGTGGCTTCAA AGTGTGTGTGCAGGGGTGGGTGTGTTAGCGTGGGTTAGGGGAACGTGTGTGCGCGTGCT GGTGGGCATGTGAGATGACTGCCGGTGAATGTGTCCACAGTTGAGAGGTTGGAGCAGG ATGAGGAATCCTGTCACCATCAATAATCACTTGTGGAGCGCCAGCTCTGCCCAAGACGCCA CCTGGGCGGACAGCCAGGAGCTCTCCATGGCCAGGCTGCCTGTGTGCATGTTCCCTGTCTGG TGCCCCTTTGCCCGCCTCCTGCAAACCTCACAGGGTCCCCACACAACAGTGCCCTCCAGAAG CAGCCCTCGGAGGCAGAGGAAGGAAAATGGGGATGGCTGGGGCTCTCTCCATCCTTTT CTCCTTGCCTTCGCATGGCTGGCCTTCCCCTCCAAAACCTCCATTCCCCTGCTGCCAGCCCC TATGGCTGGGTCTGGTTTCTTCCCTTCCCAGAGGGTCTTACTGTTCCAGGGTGGCCCCAGGG CAGGCAGGGCCACACTATGCCTGTGCCCTGGTAAAGGTGACCCCTGCCATTTACCAGCAGC AGGCAGTCTCCGTGGTTGAAGCAGACTGGATTTTTGCTCTGCCCCTGACCCCTTGTCCCTCT TTGAGGGAGGGAGCTATGCTAGGACTCCAACCTCAGGGACTCGGGTGGCCTGCGCTAGCTT CTTTTGATACTGAAAACTTTTAAGGTGGGAGGGTGGCAAGGGATGTGCTTAATAAATCAATT CCAAGCCTCAAAAAAAAAAAAAAAAAAA

-20/310

FIGURE 216

MAGLAARLVLLAGAAALASGSQGDREPVYRDCVLQCEEQNCSGGALNHFRSRQPIYMSLAGW
TCRDDCKYECMWVTVGLYLQEGHKVPQFHGKWPFSRFLFFQEPASAVASFLNGLASLVMLCR
YRTFVPASSPMYHTCVAFAWVSLNAWFWSTVFHTRDTDLTEKMDYFCASTVILHSIYLCCVR
TVGLQHPAVVSAFRALLLLMLTVHVSYLSLIRFDYGYNLVANVAIGLVNVVWWLAWCLWNQR
RLPHVRKCVVVVLLLQGLSLLELLDFPPLFWVLDAHAIWHISTIPVHVLFFSFLEDDSLYLL
KESEDKFKLD

GGCCGCCTGGAATTGTGGGAGTTGTGTCTGCCACTCGGCTGCCGGAGGCCGAAGGTCCGTGA CTATGGCTCCCCAGAGCCTGCCTTCATCTAGGATGGCTCCTCTGGGCATGCTGCGTTGGGCTG CTGATGGCCGCCTGCTTCACCTTCTGCCTCAGTCATCAGAACCTGAAGGAGTTTGCCCTGAC TGGATGCCGAAGTCCTGGAGGTGTTCCACCCGACGCATGAGTGGCAGGCCCTTCAGCCAGGG CAGGCTGTCCCTGCAGGATCCCACGTACGGCTGAATCTTCAGACTGGGGAAAGAGAGGCAAA ACTCCAATATGAGGACAAGTTCCGAAATAATTTGAAAGGCAAAAGGCTGGATATCAACACCA ACACCTACACATCTCAGGATCTCAAGAGTGCACTGGCAAAATTCAAGGAGGGGGCAGAGATG GAGAGTTCAAAGGAAGACAAGGCAAGGCAGGCTGAGGTAAAGCGGCTCTTCCGCCCCATTGA GGAACTGAAGAAAGACTTTGATGAGCTGAATGTTGTCATTGAGACTGACATGCAGATCATGG TACGGCTGATCAACAAGTTCAATAGTTCCAGCTCCAGTTTGGAAGAGAAGATTGCTGCGCTC TTTGATCTTGAATATTATGTCCATCAGATGGACAATGCGCAGGACCTGCTTTCCTTTGGTGG TCTTCAAGTGGTGATCAATGGGCTGAACAGCACAGAGCCCCTCGTGAAGGAGTATGCTGCGT TTGTGCTGGGCGCTGCCTTTTCCAGCAACCCCAAGGTCCAGGTGGAGGCCATCGAAGGGGGA GCCCTGCAGAAGCTGCTGGTCATCCTGGCCACGGAGCAGCCGCTCACTGCAAAGAAGAAGGT CCTGTTTGCACTGTGCTCCCTGCTGCGCCACTTCCCCTATGCCCAGCGGCAGTTCCTGAAGC TCGGGGGCTGCAGGTCCTGAGGACCCTGGTGCAGGAGAAGGGCACGGAGGTGCTCGCCGTG CGCGTGGTCACACTGCTCTACGACCTGGTCACGGAGAAGATGTTCGCCGAGGAGGAGGCTGA GCTGACCCAGGAGATGTCCCCAGAGAAGCTGCAGCAGTATCGCCAGGTACACCTCCTGCCAG GCCTGTGGGAACAGGGCTGGTGCGAGATCACGGCCCACCTCCTGGCGCTGCCCGAGCATGAT GCCCGTGAGAAGGTGCTGCAGACACTGGGCGTCCTCCTGACCACCTGCCGGGACCGCTACCG TCAGGACCCCCAGCTCGGCAGGACACTGGCCAGCCTGCAGGCTGAGTACCAGGTGCTGGCCA GCCTGGAGCTGCAGGATGGTGAGGACGAGGGCTACTTCCAGGAGCTGCTGGGCTCTGTCAAC AGCTTGCTGAAGGAGCTGAGA<u>TGA</u>GGCCCCACACCAGGACTGGACTGGGATGCCGCTAGTGA GGCTGAGGGGTGCCAGCGTGGGTGGGCTTCTCAGGCAGGAGGACATCTTGGCAGTGCTGGCT

MAPQSLPSSRMAPLGMLLGLLMAACFTFCLSHQNLKEFALTNPEKSSTKETERKETKAEEEL
DAEVLEVFHPTHEWQALQPGQAVPAGSHVRLNLQTGEREAKLQYEDKFRNNLKGKRLDINTN
TYTSQDLKSALAKFKEGAEMESSKEDKARQAEVKRLFRPIEELKKDFDELNVVIETDMQIMV
RLINKFNSSSSSLEEKIAALFDLEYYVHQMDNAQDLLSFGGLQVVINGLNSTEPLVKEYAAF
VLGAAFSSNPKVQVEAIEGGALQKLLVILATEQPLTAKKKVLFALCSLLRHFPYAQRQFLKL
GGLQVLRTLVQEKGTEVLAVRVVTLLYDLVTEKMFAEEEAELTQEMSPEKLQQYRQVHLLPG
LWEQGWCEITAHLLALPEHDAREKVLQTLGVLLTTCRDRYRQDPQLGRTLASLQAEYQVLAS
LELQDGEDEGYFQELLGSVNSLLKELR

ee3/310

FIGURE 219

TTCGGCTTCCGTAGAGGAAGTGGCGCGGACCTTCATTTGGGGTTTCGGTTCCCCCCCTTCCC CTTCCCCGGGGTCTGGGGGTGACATTGCACCGCGCCCCTCGTGGGGTCGCGTTGCCACCCCA CCGGCCTTCGCGCTTTTCTTGATCACTGTGGCTGGGGACCCGCTTCGCGTTATCATCCTGGT CGCAGGGGCATTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTCTGGTTCATCTTGG TCCATGTGACCGACCGGTCAGATGCCCGGCTCCAGTACGGCCTCCTGATTTTTGGTGCTGCT GTCTCTGTCCTTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGA TGAAGGGTTAGCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCT ATGTTTCTGGTCTCCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTTGGCT GATGCACTTGGGCCAGGTGTGGTTGGGATCCATGGAGACTCACCCTATTACTTCCTGACTTC AGCCTTTCTGACAGCAGCCATTATCCTGCTCCATACCTTTTGGGGGAGTTGTGTTCTTTGATG CCTGTGAGAGGAGACGGTACTGGGCTTTGGGCCTGGTGGTTGGGAGTCACCTACTGACATCG GGACTGACATTCCTGAACCCCTGGTATGAGGCCAGCCTGCTGCCCATCTATGCAGTCACTGT TTCCATGGGGCTCTGGGCCTTCATCACAGCTGGAGGGTCCCTCCGAAGTATTCAGCGCAGCC TCTTGTGTAAGGAC<u>TGA</u>CTACCTGGACTGATCGCCTGACAGATCCCACCTGCCTGTCCACTG CCCATGACTGAGCCCAGCCCCAGCCCGGGTCCATTGCCCACATTCTCTGTCTCCTTCTCGTC GGTCTACCCCACTACCTCCAGGGTTTTGCTTTGTCCTTTTGTGACCGTTAGTCTCTAAGCTT TACCAGGAGCAGCCTGGGTTCAGCCAGTCAGTGACTGGTGGGTTTGAATCTGCACTTATCCC CACCACCTGGGGACCCCCTTGTTGTGTCCAGGACTCCCCCTGTGTCAGTGCTCTGCTCTCAC CCTGCCCAAGACTCACCTCCCTTCCCCTCTGCAGGCCGACGGCAGGAGGACAGTCGGGTGAT GGTGTATTCTGCCCTGCGCATCCCACCCGAGGACTGAGGGAACCTAGGGGGGACCCCTGGGC CTGGGGTGCCCTCGTGTCCTCGCCCTGTATTTCTCCATCTCCAGTTCTGGACAGTGCAG GTTGCCAAGAAAAGGGACCTAGTTTAGCCATTGCCCTGGAGATGAAATTAATGGAGGCTCAA GGATAGATGAGCTCTGAGTTTCTCAGTACTCCCTCAAGACTGGACATCTTGGTCTTTTTCTC AGGCCTGAGGGGGAACCATTTTTGGTGTGATAAATACCCTAAACTGCCTTTTTTTCTTTTTT GAGGTGGGGGGAGGAGGTATATTGGAACTCTTCTAACCTCCTTGGGCTATATTTTCTC TCCTCGAGTTGCTCCTCATGGCTGGGCTCATTTCGGTCCCTTTCTCCTTGGTCCCAGACCTT GGGGGAAAGGAAGTAGTTTTGGGAACTGCATTACTGGAACTAATGGTTTTAACCT CCTTAACCACCAGCATCCCTCCTCTCCCCAAGGTGAAGTGGAGGGTGCTGTGGTGAGCTGGC CACTCCAGAGCTGCAGTGCCACTGGAGGAGTCAGACTACCATGACATCGTAGGGAAGGAGGG ATCATTTTCTGCTGAGGGTGGAGTGTCCCATCCTTTTAATCAAGGTGATTGTGATTTTGACT **ААААААААААААААААААААА**

-664/310

FIGURE 220

MGAAVFFGCTFVAFGPAFALFLITVAGDPLRVIILVAGAFFWLVSLLLASVVWFILVHVTDR SDARLQYGLLIFGAAVSVLLQEVFRFAYYKLLKKADEGLASLSEDGRSPISIRQMAYVSGLS FGIISGVFSVINILADALGPGVVGIHGDSPYYFLTSAFLTAAIILLHTFWGVVFFDACERRR YWALGLVVGSHLLTSGLTFLNPWYEASLLPIYAVTVSMGLWAFITAGGSLRSIQRSLLCKD

-१२**६**/३२० FIGURE 222

GACCGACCGTTCAGATGCCCGGTTCCAGTACGGCTTCCTGATTTTTGGTGCTGCTGTNTCTG
TCCTTCTACAGGAGGTGTTCCGCTTTGCCTANTACAAGCTGCTTAAGAAGGCAGATGAGGGG
TTAGCATNGCTGAGTGAGGACGGAAGATCACCCATTTCCATCCGCCAGATGGCCTATGTTTN
TGGTNTTTCCTTCGGTATCATCAGTGGTGTTTTNTCTGTTATCAATATTTTGGNTGATGCAN
TTGGGCCAGGTGTGGTTGGGATCCATGGAGANTCACCCTATTAATTCCTGAATTCAGCCTTT
NTGACAGCAGCCATTATCCTGNTCCATACCTTTTGGGGAGTTGTTTTTTGATGCCTGTGA
GAGGAG

227/310

FIGURE 223

NGTTGGAGAAGTGGCGCGGACNTTCATTTGGGGTTTCCCCCCTTTCCCCTTTCCCCG
GGGTCTGGGGTGACATTGCACGGGCCCCTCGTGGGGTCGCGTTGCCACCCCACGCGGACTCC
CCAGNTGGNGCGCCCTTCCCATTTGCCTGTCCTGGTCAGGCCCCCACCCCCCTTCCCACNTG
ACCAGCCATGGGGGCTGCGGTGTTTTTCGGCTGCACTTTCGTCGCGTTCGGCCCGGCCTTCG
CGCTTTTCTTGATCACTGTGGCTGGGGACCCGCTTCGGTTATCATCCTGGTCGCAGGGGCA
TTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTTCATCTTTGGTCCATGTGAC
CGACCGGTCAGATGCCCGGCTCCAGTACGGCCTCCTGATTTTTGGTGCTGCTGTCTCTGTCC
TTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGATGAGGGGTTA
GCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCTATGTTTCTGG
TCTCTCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTTTGGCTGATGCACTTG
GGCCAGGTGTGGGTTGGGATCCATCGAGAGCTCACCC

-ee8/310

FIGURE 224

WO 99/63088

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GCCCCAGGGAGCAGTGGGTGTTATAACTCAGGCCCGGTGCCCAGAGCCCAGGAGGAGGCAG TGGCCAGGAAGGCACAGGCCTGAGAAGTCTGCGGCTGAGCTGGGAGCAAATCCCCCACCCCC TGTCTGTGCGTCCTGCACCCACATCTTTCTCTGTCCCCTCCTTGCCCTGTCTGGAGGCTGCT AGACTCCTATCTTCTGAATTCTATAGTGCCTGGGTCTCAGCGCAGTGCCGATGGTGGCCCGT $\tt CCTTGTGGTTCCTCTCTACCTGGGGAAATAAGGTGCAGCGGCC\underline{ATG}GCTACAGCAAGACCCCC$ CCTGGATGTGGGTGCTCTGTGCTCTGATCACAGCCTTGCTTCTGGGGGTCACAGAGCATGTT CTCGCCAACAATGATGTTTCCTGTGACCACCCCTCTAACACCGTGCCCTCTGGGAGCAACCA GGACCTGGGAGCTGGGGCCGGGGAAGACGCCCGGTCGGATGACAGCAGCAGCCGCATCATCA ATGGATCCGACTGCGATATGCACACCCAGCCGTGGCAGGCCGCGCTGTTGCTAAGGCCCAAC CAGCTCTACTGCGGGGCGGTGTTGGTGCATCCACAGTGGCTGCTCACGGCCGCCCCACTGCAG GAAGAAAGTTTTCAGAGTCCGTCTCGGCCACTACTCCCTGTCACCAGTTTATGAATCTGGGC AGCAGATGTTCCAGGGGGTCAAATCCATCCCCCACCCTGGCTACTCCCACCCTGGCCACTCT AACGACCTCATGCTCATCAAACTGAACAGAAGAATTCGTCCCACTAAAGATGTCAGACCCAT CCAAGAGCCCCCAAGTGCACTTCCCTAAGGTCCTCCAGTGCTTGAATATCAGCGTGCTAAGT CAGAAAAGGTGCGAGGATGCTTACCCGAGACAGATAGATGACACCATGTTCTGCGCCGGTGA CAAAGCAGGTAGAGACTCCTGCCAGGGTGATTCTGGGGGGGCCTGTGGTCTGCAATGGCTCCC TGCAGGGACTCGTGTCCTGGGGAGATTACCCTTGTGCCCGGCCCAACAGACCGGGTGTCTAC ACGAACCTCTGCAAGTTCACCAAGTGGATCCAGGAAACCATCCAGGCCAACTCCTGAGTCAT CCCAGGACTCAGCACACCGGCATCCCCACCTGCTGCAGGGACAGCCCTGACACTCCTTTCAG ACCCTCATTCCTTCCCAGAGATGTTGAGAATGTTCATCTCTCCAGCCCCTGACCCCATGTCT CCTGGACTCAGGGTCTGCTTCCCCCACATTGGGCTGACCGTGTCTCTAGTTGAACCCTGG GAACAATTTCCAAAACTGTCCAGGGCGGGGGTTGCGTCTCAATCTCCCTGGGGCACTTTCAT CCTCAAGCTCAGGGCCCATCCCTTCTCTGCAGCTCTGACCCAAATTTAGTCCCAGAAATAAA CTGAGAAGTGGAAAAAAAAA

MATARPPWMWVLCALITALLLGVTEHVLANNDVSCDHPSNTVPSGSNQDLGAGAGEDARSDD SSSRIINGSDCDMHTQPWQAALLLRPNQLYCGAVLVHPQWLLTAAHCRKKVFRVRLGHYSLS PVYESGQQMFQGVKSIPHPGYSHPGHSNDLMLIKLNRRIRPTKDVRPINVSSHCPSAGTKCL VSGWGTTKSPQVHFPKVLQCLNISVLSQKRCEDAYPRQIDDTMFCAGDKAGRDSCQGDSGGP VVCNGSLQGLVSWGDYPCARPNRPGVYTNLCKFTKWIQETIQANS

WO 99/63088

-031/310

FIGURE 227

<u>ATG</u>GTCAACGACCGGTGGAAGACCATGGGCGGCGCTGCCCAACTTGAGGACCGGCCGCGCGA CAAGCCGCAGCCGAGCTGCGGCTACGTGCTGCACCGTGCTGCTGCCTGGCTGTGC TGCTGGCTGTAGCTGTCACCGGTGCCGTGCTCTTCCTGAACCACGCCCACGCCCCGGGCACG GCGCCCCACCTGTCGTCAGCACTGGGGCTGCCAGCGCCAACAGCGCCCTGGTCACTGTGGA AAGGGCGGACAGCTCGCACCTCAGCATCCTCATTGACCCGCGCTGCCCCGACCTCACCGACA GCTTCGCACGCCTGGAGAGCGCCCAGGCCTCGGTGCTGCAGGCGCTGACAGAGCACCAGGCC CAGCCACGGCTGGTGGGCGACCAGGAGCAGGAGCTGCTGGACACGCTGGCCGACCAGCTGCC CCGGCTGCTGGCCCGAGCCTCAGAGCTGCAGACGGAGTGCATGGGGCTGCGGAAGGGGCATG GCACGCTGGGCCAGGGCCTCAGCGCCCTGCAGAGTGAGCAGGGCCGCCTCATCCAGCTTCTC TCTGAGAGCCAGGGCCACATGGCTCACCTGGTGAACTCCGTCAGCGACATCCTGGATGCCCT GCAGAGGGACCGGGGCTGGGCCCGGCCCCGCAACAAGGCCGACCTTCAGAGAGCGCCTGCCC GGGGAACCCGGCCCCGGGCTGTGCCACTGGCTCCCGGCCCCGAGACTGTCTGGACGTCCTC CCAGGTGTACTGTGACATGCGCACGGACGGCGGCGGCTGGACGGTGTTTCAGCGCCGGGAGG ACGGCTCCGTGAACTTCTTCCGGGGCTGGGACGCGTACCGAGACGGCTTTGGCAGGCTCACC GGGGAGCACTGGCTAGGGCTCAAGAGGATCCACGCCCTGACCACACAGGCTGCCTACGAGCT GCACGTGGACCTGGAGGACTTTGAGAATGGCACGGCCTATGCCCGCTACGGGAGCTTCGGCG TGGGCTTGTTCTCCGTGGACCCTGAGGAAGACGGGTACCCGCTCACCGTGGCTGACTATTCC GGCACTGCAGGCGACTCCCTCCTGAAGCACAGGGCGCATGAGGTTCACCACCAAGGACCGTGA CAGCGACCATTCAGAGAACAACTGTGCCGCCTTCTACCGCGGTGCCTGGTGCTACCGCAACT GCCACACGTCCAACCTCAATGGGCAGTACCTGCGCGGTGCGCACGCCTCCTATGCCGACGGC ${\tt GCCGGTCCGGGAGGACCGC\underline{TAG}ACTGGTGCACCTTGTCCTTGGCCCTGGTCCCTGTCGC}$ CCACTCTCCAGTAGGGAGGGCCGGGCCATCCCTGACACGAAGCTCCCTGGGCCGGTGAAGT CACACATCGCCTTCTCGCCGTCCCCACCCCCTCCATTTGGCAGCTCACTGATCTCTTGCCTC TGCTGTTTGCCGTCCCCTGGCCAGGATGGTGGAGTCTGCCCCAGGCACCCTCTGCCCTGCCC GGCCAAATACCCGGCATTATGGGGACAGAGAGCAGGGGGGCAGACAGCACCCCTGGAGTCCTC CTAGCAGATCGTGGGGAATGTCAGGTCTCTCTGAGGTCAGGTCTGAGGCCAGTATCCTCCAG CCCTCCCAATGCCAACCCCCACCCCGTTTCCCTGGTGCCCAGAGAACCCACCTCTCCCCCAA GGGCCTCAGCCTGGCTGGGCTGGGTGGCCCCATCCTACCAGGCCCTGAGGTCAGGATGGG CCTGTGCCCCGGCAGGCCTGGGGTCTGCAGTCCTCTTACCTGCTGTGCCCACCTGCTCTCTG TCTCAAATGAGGCCCAACCCATCCCCCACCCAGCTCCCGGCCGTCCTCCTACCTGGGGCAGC GGACTGCGCTAATGGGAAGCTCTTGGTTTTCTGGGCTGGGGCCTAGGCAGGGCTGGGATGAG GCTTGTACAACCCCCACCACCAATTTCCCCAGGGACTCCAGGGTCCTGAGGCCTCCCAGGAGG GCCTTGGGGGTGATGACCCCTTCCCTGAGGTGGCTGTCTCCATGAGGAGGCCAACCCTTGCC CCACCTCACCGGGCAAATGGGGTCGGGGGGACTGGGGCACCAGGCACCACCTGGACA CTTTCTTGTTGAATCCTCCCAACACCCAGCACGCTGTCATCCCCACTCCTTGTGTGCACACA TGCAGAGGTGAGACCCGCAGGCTCCCAGGACCAGCAGCCACAAGGGCAGGGCTGGAGCCGGG CGGCTTTTCCAAGGCCTCCTGATGGGGGCCTCCGAAAGGGCTGGAGTCAGCCTTGGGGAGCT GCCTAGCAGCCTCTCCTCGGGCAGGAGGGGGGGGTGGCTTCCTCCAAAGGACACCCGATGGCA GGTGCCTAGGGGGTGTGGGGTTCCGTTCTCCCTTCCCCTCCCACTGAAGTTTGTGCTTAAAA AACAATAAATTTGACTTGGCACCACTGGGGGGTTGGTGGGAGAGGCCGTGTGACCTGGCTCTC TGTCCCAGTGCCACCAGGTCATCCACATGCGCAG

-e32/310

FIGURE 228

MVNDRWKTMGGAAQLEDRPRDKPQRPSCGYVLCTVLLALAVLLAVAVTGAVLFLNHAHAPGT
APPPVVSTGAASANSALVTVERADSSHLSILIDPRCPDLTDSFARLESAQASVLQALTEHQA
QPRLVGDQEQELLDTLADQLPRLLARASELQTECMGLRKGHGTLGQGLSALQSEQGRLIQLL
SESQGHMAHLVNSVSDILDALQRDRGLGRPRNKADLQRAPARGTRPRGCATGSRPRDCLDVL
LSGQQDDGVYSVFPTHYPAGFQVYCDMRTDGGGWTVFQRREDGSVNFFRGWDAYRDGFGRLT
GEHWLGLKRIHALTTQAAYELHVDLEDFENGTAYARYGSFGVGLFSVDPEEDGYPLTVADYS
GTAGDSLLKHSGMRFTTKDRDSDHSENNCAAFYRGAWWYRNCHTSNLNGQYLRGAHASYADG
VEWSSWTGWQYSLKFSEMKIRPVREDR

GCAGTCAGAGACTTCCCCTGCCCCTCGCTGGGAAAGAACATTAGGAATGCCTTTTAGTGCCT TGCTTCCTGAACTAGCTCACAGTAGCCCGGCGGCCCAGGGCAATCCGACCACATTTCACTCT CACCGCTGTAGGAATCCAG<u>ATG</u>CAGGCCAAGTACAGCAGCACGAGGGACATGCTGGATGATG ATGGGGACACCACCATGAGCCTGCATTCTCAAGCCTCTGCCACAACTCGGCATCCAGAGCCC CGGCGCACAGAGCACAGGGCTCCCTCTTCAACGTGGCGACCAGTGGCCCTGACCCTGAC TTTGTGCTTGGTGCTGATAGGGCTGGCAGCCCTGGGGCTTTTGTTTTTCAGTACTACC AGCTCTCCAATACTGGTCAAGACACCATTTCTCAAATGGAAGAAGATTAGGAAATACGTCC CAAGAGTTGCAATCTCTTCAAGTCCAGAATATAAAGCTTGCAGGAAGTCTGCAGCATGTGGC TGAAAAACTCTGTCGTGAGCTGTATAACAAAGCTGGAGCACACAGGTGCAGCCCTTGTACAG AACAATGGAAATGGCATGGAGACAATTGCTACCAGTTCTATAAAGACAGCAAAAGTTGGGAG ${\tt CCTGGAATTTGCCGCGTCTCAGAGCTACTCTGAGTTTTTCTACTCTTATTGGACAGGGCTTT}$ TTCCATATTATAATAGATGTCACCAGCCCAAGAAGCAGAGACTGTGTGGCCCATCCTCAATGG GATGATCTTCTCAAAGGACTGCAAAGAATTGAAGCGTTGTGTCTGTGAGAGAAGGGCAGGAA TGGTGAAGCCAGAGAGCCTCCATGTCCCCCCTGAAACATTAGGCGAAGGTGAC<u>TGA</u>TTCGCC CTCTGCAACTACAAATAGCAGAGTGAGCCAGGCGGTGCCAAAGCAAGGGCTAGTTGAGACAT TGGGAAATGGAACATAATCAGGAAAGACTATCTCTCTGACTAGTACAAAATGGGTTCTCGTG TTTCCTGTTCAGGATCACCAGCATTTCTGAGCTTGGGTTTATGCACGTATTTAACAGTCACA AGAAGTCTTATTTACATGCCACCAACCAACCTCAGAAACCCATAATGTCATCTGCCTTCTTG GCTTAGAGATAACTTTTAGCTCTCTTTCTTCTCAATGTCTAATATCACCTCCCTGTTTTCAT GTCTTCCTTACACTTGGTGGAATAAGAAACTTTTTGAAGTAGAGGAAATACATTGAGGTAAC ${\tt ATCCTTTTCTCTGACAGTCAAGTAGTCCATCAGAAATTGGCAGTCACTTCCCAGATTGTACC}$ AGCAAATACACAAGGAATTCTTTTTGTTTGTTTCAGTTCATACTAGTCCCTTCCCAATCCAT CAGTAAAGACCCCATCTGCCTTGTCCATGCCGTTTCCCAACAGGGATGTCACTTGATATGAG AATCTCAAATCTCAATGCCTTATAAGCATTCCTTCCTGTGTCCATTAAGACTCTGATAATTG TCTCCCCTCCATAGGAATTTCTCCCAGGAAAGAAATATATCCCCATCTCCGTTTCATATCAG AACTACCGTCCCCGATATTCCCTTCAGAGAGATTAAAGACCAGAAAAAAGTGAGCCTCTTCA TCTGCACCTGTAATAGTTTCAGTTCCTATTTTCTTCCATTGACCCATATTTATACCTTTCAG GTACTGAAGATTTAATAATAATAAATGTAAATACTGTGAAAAA

231/310

FIGURE 230

MQAKYSSTRDMLDDDGDTTMSLHSQASATTRHPEPRRTEHRAPSSTWRPVALTLLTLCLVLL IGLAALGLLFFQYYQLSNTGQDTISQMEERLGNTSQELQSLQVQNIKLAGSLQHVAEKLCRE LYNKAGAHRCSPCTEQWKWHGDNCYQFYKDSKSWEDCKYFCLSENSTMLKINKQEDLEFAAS QSYSEFFYSYWTGLLRPDSGKAWLWMDGTPFTSELFHIIIDVTSPRSRDCVAILNGMIFSKD CKELKRCVCERRAGMVKPESLHVPPETLGEGD

~35/310 FIGURE 231

236/310

FIGURE 232

GCCGAGCGCAAGAACCCTGCGCAGCCCAGAGCAGCTGCTGGAGGGGAATCGAGGCGCGGCTC CTGGGGGTTCGCCGGGGCCGGGGACCCGCGGTCCGGGCGCCATGCGGGCATCGCTGCTG TCGGTGCTGCGGCCCGCAGGGCCCGTGGCCGTGGGCATCTCCCTGGGCTTCACCCTGAGCCT GCTCAGCGTCACCTGGGTGGAGGAGCCGTGCGGCCCAGGCCCCCAACCTGGAGACTCTG AGCTGCCGCCGCGCGAACACCAACGCGGCGCGCCCGACTCGGTGCAGCCCGGAGCG GAGCGCGAGAAGCCCGGGGCCGGCGAAGGCGCCGGGGAGAATTGGGAGCCGCGCGTCTTGCC CTACCACCCTGCACAGCCCGGCCAGGCCGCCAAAAAGGCCGTCAGGACCCGCTACATCAGCA CGGAGCTGGGCATCAGGCAGAGGCTGCTGGTGGCGGTGCTGACCTCTCAGACCACGCTGCCC ACGCTGGGCGTGGACCGCACGCTGGGGCACCGGCTGGAGCGTGTGGTGTTCCTGAC GGGCGCACGGGGCCCCGGGCCCCACCTGGCATGGCAGTGGTGACGCTGGGCGAGGAGCGAC CCATTGGACACCTGCACCTGCGCGCCACCTGCTGGAGCAGCACGGCGACGACTTTGAC TGGTTCTTCCTGGTGCCTGACACCACCTACACCGAGGCGCACGGCCTGGCACGCCTAACTGG GAGAGCCCACCCCGGCCGCTACTGCCACGGAGGCTTTGGGGTGCTGCTGTCGCGCATGCTG CTGCAACAACTGCGCCCCCACCTGGAAGGCTGCCGCAACGACATCGTCAGTGCGCGCCCTGA CGAGTGGCTGGGTCGCTGCATTCTCGATGCCACCGGGGTGGGCTGCACTGGTGACCACGAGG GGGTGCACTATAGCCATCTGGAGCTGAGCCCTGGGGAGCCAGTGCAGGAGGGGGACCCTCAT TTCCGAAGTGCCCTGACAGCCCACCCTGTGCGTGACCCTGTGCACATGTACCAGCTGCACAA AGCTTTCGCCCGAGCTGAACTGGAACGCACGTACCAGGAGATCCAGGAGTTACAGTGGGAGA TCCAGAATACCAGCCATCTGGCCGTTGATGGGGACCGGGCAGCTGCTTGGCCCGTGGGTATT CCAGCACCATCCCGCCCGGCCTCCCGCTTTGAGGTGCTGCGCTGGGACTACTTCACGGAGCA GCACGCTTTCTCCTGCGCCGATGGCTCACCCCGCTGCCCACTGCGTGGGGCTGACCGGGCTG ATGTGGCCGATGTTCTGGGGACAGCTCTAGAGGAGCTGAACCGCCGCTACCACCCGGCCTTG CGGCTCCAGAAGCAGCAGCTGGTGAATGGCTACCGACGCTTTGATCCGGCCCGGGGTATGGA ATACÁCGCTGGACTTGCAGCTGGAGGCACTGACCCCCCAGGGAGGCCGCCGGCCCCTCACTC GCCGAGTGCAGCTGCTCCGGCCGCTGAGCCGCGTGGAGATCTTGCCTGTGCCCTATGTCACT GAGGCCTCACGTCTCACTGTGCTGCTGCCTCTAGCTGCGGCTGAGCGTGACCTGGCCCCTGG CTTCTTGGAGGCCTTTGCCACTGCAGCACTGGAGCCTGGTGATGCTGCGGCAGCCCTGACCC TGCTGCTACTGTATGAGCCGCGCCAGGCCCAGCGCGTGGCCCATGCAGATGTCTTCGCACCT GTCAAGGCCCACGTGGCAGAGCTGGAGCGGCGTTTCCCCGGTGCCCGGGTGCCATGGCTCAG TGTGCAGACAGCCGCACCCTCACCACTGCGCCTCATGGATCTACTCTCCAAGAAGCACCCGC TGGACACACTGTTCCTGCTGGCCGGGCCAGACACGGTGCTCACGCCTGACTTCCTGAACCGC TGCCGCATGCATGCCATCTCCGGCTGGCAGGCCTTCTTTCCCATGCATTTCCAAGCCTTCCA CCCAGGTGTGGCCCCACCACAAGGGCCTGGGCCCCCAGAGCTGGGCCGTGACACTGGCCGCT TTGATCGCCAGGCAGCCAGCGAGGCCTGCTTCTACAACTCCGACTACGTGGCAGCCCGTGGG CGCCTGGCGGCAGCCTCAGAACAAGAAGAGGGGCTGCTGGAGAGCCTGGATGTGTACGAGCT GTTCCTCCACTTCTCCAGTCTGCATGTGCTGCGGGCGGTGGAGCCGGCGCTGCTGCAGCGCT ACCGGGCCCAGACGTGCAGCGCGAGGCTCAGTGAGGACCTGTACCACCGCTGCCTCCAGAGC GTGCTTGAGGGCCTCGGCTCCCGAACCCAGCTGGCCATGCTACTCTTTGAACAGGAGCAGGG ${\tt CAACAGCACC} {\tt TGA} {\tt CCCCACCCTGTCCCCGTGGGCCGTGGCCATGGCCACCCCACCCCACTT}$ CTCCCCAAAACCAGAGCCACCTGCCAGCCTCGCTGGGCAGGGCTGGCCGTAGCCAGACCCC AAGCTGGCCCACTGGTCCCCTCTCTGGCTCTGTGGGTCCCTGGGCTCTGGACAAGCACTGGG GGACGTGCCCCAGAGCCACCCACTTCTCATCCCAAACCCAGTTTCCCTGCCCCCTGACGCT GCTGATTCGGGCTGTGGCCTCCACGTATTTATGCAGTACAGTCTGCCTGACGCCAGCCCTGC CTCTGGGCCCTGGGGCTGGGCTGTAGAAGAGTTGTTGGGGAAGGAGGAGCTGAGGAGGG GCATCTCCCAACTTCTCCCTTTTGGACCCTGCCGAAGCTCCCTGCCTTTAATAAACTGGCCA **AGTGTGGAAAAA**

MRASILLSVLRPAGPVAVGISLGFTLSLLSVTWVEEPCGPGPPQPGDSELPPRGNTNAARRP
NSVQPGAEREKPGAGEGAGENWEPRVLPYHPAQPGQAAKKAVRTRY ISTELGIRQRLLVAVL
TSQTTLPTLGVAVNRTLGHRLERVVFLTGARGRRAPPGMAVVTLGEERPIGHLHLALRHLLE
QHGDDFDWFFLVPDTTYTEAHGLARLTGHLSLASAAHLYLGRPQDFIGGEPTPGRYCHGGFG
VLLSRMLLQQLRPHLEGCRNDIVSARPDEWLGRCILDATGVGCTGDHEGVHYSHLELSPGEP
VQEGDPHFRSALTAHPVRDPVHMYQLHKAFARAELERTYQEIQELQWEIQNTSHLAVDGDRA
AAWPVGIPAPSRPASRFEVLRWDYFTEQHAFSCADGSPRCPLRGADRADVADVLGTALEELN
RRYHPALRLQKQQLVNGYRRFDPARGMEYTLDLQLEALTPQGGRRPLTRRVQLLRPLSRVEI
LPVPYVTEASRLTVLLPLAAAERDLAPGFLEAFATAALEPGDAAAALTLLLLYEPRQAQRVA
HADVFAPVKAHVAELERRFPGARVPWLSVQTAAPSPLRLMDLLSKKHPLDTLFLLAGPDTVL
TPDFLNRCRMHAISGWQAFFPMHFQAFHPGVAPPQGPGPPELGRDTGRFDRQAASEACFYNS
DYVAARGRLAAASEQEEELLESLDVYELFLHFSSLHVLRAVEPALLQRYRAQTCSARLSEDL
YHRCLQSVLEGLGSRTQLAMLLFEQEQGNST

~38 /310 FIGURE 234

GCTCTGGCCGGCCCCGGCGATTGGTCACCGCCCGCTAGGGGACAGCCCTGGCCTCCTCTGAT TGGCAAGCGCTGGCCACCCCCCACACCCCTTGCGAACGCTCCCCTAGTGGAGAAAAGGAGT AGCTATTAGCCAATTCGGCAGGGCCCGCTTTTTAGAAGCTTGATTTCCTTTGAAGATGAAAG ACTAGCGGAAGCTCTGCCTCTTTCCCCAGTGGGCGAGGGAACTCGGGGCGATTGGCTGGGAA CTGTATCCACCCAAATGTCACCGATTTCTTCCTATGCAGGAAATGAGCAGACCCATCAATAA GAAATTTCTCAGCCTGGCCGAAAATGGTTGGCCCCACGAAGCCACGACAACTGGAGGCAAAG AGGGTTGCTCAACGCCCCGCCTCATTGGAAAACCAAATCAGATCTGGGACCTATATAGCGTG GCGGAGGCGGGCGATGATTGTCGCGCTCGCACCCACTGCAGCTGCGCACAGTCGCATTTCT ATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCCGCTGTGGCGGGAAAGCGGCCCCCAGAAC CGACCACACCGTGGCAAGAGGACCCAGAACCCGAGGACGAAAACTTGTATGAGAAGAACCCA GACTCCCATGGTTATGACAAGGACCCCGTTTTGGACGTCTGGAACATGCGACTTGTCTTCTT CTTTGGCGTCTCCATCATCCTGGTCCTTGGCAGCACCTTTGTGGCCTATCTGCCTGACTACA GGATGAAAGAGTGGTCCCGCCGCGAAGCTGAGAGGCTTGTGAAATACCGAGAGGCCAATGGC $\tt CTTCCCATCATGGAATCCAACTGCTTCGACCCCAGCAAGATCCAGCTGCCAGAGGATGAG{\color{red}{\bf TG}}$ CTCTTCTCAGAGCACCTAATTAAAGGGGCTGAAAGTCTGAA

MAAGLFGLSARRLLAAAATRGLPAARVRWESSFSRTVVAPSAVAGKRPPEPTTPWQEDPEPE DENLYEKNPDSHGYDKDPVLDVWNMRLVFFFGVSIILVLGSTFVAYLPDYRMKEWSRREAER LVKYREANGLPIMESNCFDPSKIQLPEDE

~ 40/310 FIGURE 236

GGCGGCTGGGCTGTTTGGTTTGAGCGCTCGCCGTCTTTTTGGCGGCAGCGCGACGCGAGGGC
TCCCGGCCGCCCCGCGTCCGCTGGGAATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCCGCT
GTGGCGGGAAAGCGGCCCCCAGAACCGACCACACCGTGGCAAGAGGACCCAGAACCCGAGGA
CGAAAACTTGTATGAGAAGAACCCAGACTCCCATGGTTATGACAAGGACCCCGTTTTGGACG
TCTGGAACATGCGACTTGTCTTCTTTCTTTTGGCGTCTCCATCATCCTGGTCCTTGGCAGCACC
TTTGTGGCCTATCTGCCTGACTACAGGATGAAAGAGTGGTCCCGCCGCGAAGCTGAGAGGCT
TGTGAAATACCGAGAGGCCCAATGGCCTTCCCATCATGGAATCCAACTGCTTCGACCCCAGCA
AGATCCAG

~41/310 FIGURE 237

GCGGCGGCT<u>ATG</u>CCGCTTGCTCTGCTCCTGTTGCTCCTGGGGCCCGGCGGCTGGTGCCT TGCAGAACCCCCACGCGACAGCCTGCGGGAGGAACTTGTCATCACCCCGCTGCCTTCCGGGG ACGTAGCCGCCACATTCCAGTTCCGCACGCGCTGGGATTCGGAGCTTCAGCGGGAAGGAGTG TCCCATTACAGGCTCTTTCCCAAAGCCCTGGGGCAGCTGATCTCCAAGTATTCTCTACGGGA GCTGCACCTGTCATTCACACAAGGCTTTTGGAGGACCCGATACTGGGGGCCCACCCTTCCTGC AGGCCCCATCAGGTGCAGAGCTGTGGGTCTGGTTCCAAGACACTGTCACTGATGTGGATAAA TCTTGGAAGGAGCTCAGTAATGTCCTCTCAGGGATCTTCTGCGCCTCTCTCAACTTCATCGA CTCCACCAACACAGTCACTCCCACTGCCTCCTTCAAACCCCTGGGTCTGGCCAATGACACTG ACCACTACTTTCTGCGCTATGCTGTGCCGCGGGGGGGTGGTCTGCACCGAAAACCTCACC CCCTGGAAGAAGCTCTTGCCCTGTAGTTCCAAGGCAGGCCTCTCTGTGCTGCTGAAGGCAGA TCGCTTGTTCCACACCAGCTACCACTCCCAGGCAGTGCATATCCGCCCTGTTTGCAGAAATG CACGCTGTACTAGCATCTCCTGGGAGCTGAGGCAGACCCTGTCAGTTGTATTTGATGCCTTC ATCACGGGCAGGGAAAGAAGACTGGTCCCTCTTCCGGATGTTCTCCCGAACCCTCACGGA GCCCTGCCCCTGGCTTCAGAGAGCCGAGTCTATGTGGACATCACCACCTACAACCAGGACA ACGAGACATTAGAGGTGCACCCACCCCGACCACTACATATCAGGACGTCATCCTAGGCACT CGGAAGACCTATGCCATCTATGACTTGCTTGACACCGCCATGATCAACAACTCTCGAAACCT CAACATCCAGCTCAAGTGGAAGAGACCCCCAGAGAATGAGGCCCCCCAGTGCCCTTCCTGC ATGCCCAGCGGTACGTGAGTGGCTATGGGCTGCAGAAGGGGGAGCTGAGCACACTGCTGTAC AACACCCACCCATACCGGGCCTTCCCGGTGCTGCTGCTGGACACCGTACCCTGGTATCTGCG GCTGTATGTGCACACCCTCACCATCACCTCCAAGGGCAAGGAGAACAAACCAAGTTACATCC ACTACCAGCCTGCCAGGACCGGCTGCAACCCCACCTCCTGGAGATGCTGATTCAGCTGCCG GCCAACTCAGTCACCAAGGTTTCCATCCAGTTTGAGCGGGCGCTGCTGAAGTGGACCGAGTA CACGCCAGATCCTAACCATGGCTTCTATGTCAGCCCATCTGTCCTCAGCGCCCTTGTGCCCA GCATGGTAGCAGCCAAGCCAGTGGACTGGGAAGAGAGTCCCCTCTTCAACAGCCTGTTCCCA GTCTCTGATGGCTCTAACTACTTTGTGCGGCTCTACACGGAGCCGCTGCTGGAACCTGCC GACACCGGACTTCAGCATGCCCTACAACGTGATCTGCCTCACGTGCACTGTGGTGGCCGTGT GCTACGGCTCCTTCTACAATCTCCTCACCCGAACCTTCCACATCGAGGAGCCCCGCACAGGT ${\tt GGCCTGGCCAAGCGGCGAACCTTATCCGGCGCGCCCGAGGTGTCCCCCCACTC}$ $\tt CTTGCCCTTTCCAGCAGCTGCAGCTGCCGTTTCTCTCTGGGGAGGGGAGCCCAAGGGCTGTT$ TCTGCCACTTGCTCTCCTCAGAGTTGGCTTTTGAACCAAAGTGCCCTGGACCAGGTCAGGGC CTACAGCTGTGTTGTCCAGTACAGGAGCCACGAGCCAAATGTGGCATTTGAATTTAA CTTAGAAATTCATTTCCTCACCTGTAGTGGCCACCTCTATATTGAGGTGCTCAATAAGCAAA AGTGGTCGGTGGCTGCTGTATTGGACAGCACAGAAAAAGATTTCCATCACCACAGAAAGGTC GGCTGGCAGCACTGGCCAAGGTGATGGGGTGTGCTACACAGTGTATGTCACTGTGTAGTGGA

FIGURE 238

MPLALLVLLLLGPGGWCLAEPPRDSLREELVITPLPSGDVAATFQFRTRWDSELQREGVSHY
RLFPKALGQLISKYSLRELHLSFTQGFWRTRYWGPPFLQAPSGAELWVWFQDTVTDVDKSWK
ELSNVLSGIFCASLNFIDSTNTVTPTASFKPLGLANDTDHYFLRYAVLPREVVCTENLTPWK
KLLPCSSKAGLSVLLKADRLFHTSYHSQAVHIRPVCRNARCTSISWELRQTLSVVFDAFITG
QGKKDWSLFRMFSRTLTEPCPLASESRVYVDITTYNQDNETLEVHPPPTTTYQDVILGTRKT
YAIYDLLDTAMINNSRNLNIQLKWKRPPENEAPPVPFLHAQRYVSGYGLQKGELSTLLYNTH
PYRAFPVLLLDTVPWYLRLYVHTLTITSKGKENKPSYIHYQPAQDRLQPHLLEMLIQLPANS
VTKVSIQFERALLKWTEYTPDPNHGFYVSPSVLSALVPSMVAAKPVDWEESPLFNSLFPVSD
GSNYFVRLYTEPLLVNLPTPDFSMPYNVICLTCTVVAVCYGSFYNLLTRTFHIEEPRTGGLA
KRLANLIRRARGVPPL

WO 99/63088

~43/310 FIGURE 239

FIGURE 240

 ${\tt MGSSSFLVLMVSLVLVTLVAVEGVKEGIEKAGVCPADNVRCFKSDPPQCHTDQDCLGERKCC} \\ {\tt YLHCGFKCVIPVKELEEGGNKDEDVSRPYPEPGWEAKCPGSSSTRCPQK} \\$

FIGURE 241

AAACTCAGCACTTGCCGGAGTGGCTCATTGTTAAGACAAAGGGTGTGCACTTCCTGGCCAGG AAACCTGAGCGGTGAGACTCCCAGCTGCCTACATCAAGGCCCCAGGACATGCAGAACCTTCC TCTAGAACCCGACCCACCATGAGGTCCTGCCTGTGGAGATGCAGGCACCTGAGCCAAGG CTACAGTCCCTGGCAAAGCCTAAGTCCCAGGCACCCACAAGGGCGAGGAGGACAACCATCTA TGCAGAGCCAGCGCCAGAGAACAATGCCCTCAACACACAAACCCAGCCCAAGGCCCACACCA ACAGCACAGAGGGCAGCATGGAAGAGCCCCAGAAAAAGAGAAAACCATGGTGAACACACTGTC ACCCAGAGGGCAAGATGCAGGGATGGCCTCTGGCAGGACAGAGGCACAATCATGGAAGAGCC AGGACACAAAGACGACCCAAGGAAATGGGGGCCAGACCAGGAAGCTGACGGCCTCCAGGACG GTGTCAGAGAAGCACCAGGGCAAAGCGGCAACCACAGCCAAGACGCTCATTCCCAAAAGTCA GCACAGAATGCTGGCTCCCACAGGAGCAGTGTCAACAAGGACGAGACAGAAAGGAGTGACCA CAGCAGTCATCCCACCTAAGGAGAAGAACCTCAGGCCACCCCACCCCTGCCCCTTTCCAG AGCCCCACGACGCAGAGAACCAAAGACTGAAGGCCGCCAACTTCAAATCTGAGCCTCGGTG GGATTTTGAGGAAAAATACAGCTTCGAAATAGGAGGCCTTCAGACGACTTGCCCTGACTCTG TGAAGATCAAAGCCTCCAAGTCGCTGTGGCTCCAGAAACTCTTTCTGCCCAACCTCACTCTC TTCCTGGACTCCAGACACTTCAACCAGAGTGAGTGGGACCGCCTGGAACACTTTGCACCACC CTTTGGCTTCATGGAGCTCAACTACTCCTTGGTGCAGAAGGTCGTGACACGCTTCCCTCCAG TGCCCCAGCAGCAGCTGCTCCTGGCCAGCCTCCCCGCTGGGAGCCTCCGGTGCATCACCTGT GCCGTGGTGGGCAACGGGGCATCCTGAACAACTCCCACATGGGCCAGGAGATAGACAGTCA CGACTACGTGTTCCGATTGAGCGGAGCTCTCATTAAAGGCTACGAACAGGATGTGGGGACTC GGACATCCTTCTACGGCTTTACCGCCTTCTCCCTGACCCAGTCACTCCTTATATTGGGCAAT CGGGGTTTCAAGAACGTGCCTCTTGGGAAGGACGTCCGCTACTTGCACTTCCTGGAAGGCAC CCGGGACTATGAGTGGCTGGAAGCACTGCTTATGAATCAGACGGTGATGTCAAAAAACCTTT TCTGGTTCAGGCACAGACCCCAGGAAGCTTTTCGGGAAGCCCTGCACATGGACAGGTACCTG TTGCTGCACCCAGACTTTCTCCGATACATGAAGAACAGGTTTCTGAGGTCTAAGACCCTGGA TGGTGCCCACTGGAGGATATACCGCCCCACCACTGGGGCCCTCCTGCTGCTCACTGCCCTTC AGCTCTGTGACCAGGTGAGTGCTTATGGCTTCATCACTGAGGGCCATGAGCGCTTTTCTGAT CACTACTATGATACATCATGGAAGCGGCTGATCTTTTACATAAACCATGACTTCAAGCTGGA GAGAGAAGTCTGGAAGCGGCTACACGATGAAGGGATAATCCGGCTGTACCAGCGTCCTGGTC $\tt CCGGAACTGCCAAAGCCAAGAAC\underline{TGA}CCGGGGCCAGGGCTGCCATGGTCTCCTTGCCTGCTC$ CAAGGCACAGGATACAGTGGGAATCTTGAGACTCTTTGGCCATTTCCCATGGCTCAGACTAA GCTCCAAGCCCTTCAGGAGTTCCAAGGGAACACTTGAACCATGGACAAGACTCTCTCAAGAT GGCAAATGGCTAATTGAGGTTCTGAAGTTCTTCAGTACATTGCTGTAGGTCCTGAGGCCAGG GATTTTTAATTAAATGGGGTGATGGGTGGCCAATACCACAATTCCTGCTGAAAAAACACTCTT CCAGTCCAAAAGCTTCTTGATACAGAAAAAAGAGCCTGGATTTACAGAAACATATAGATCTG GTTTGAATTCCAGATCGAGTTTACAGTTGTGAAATCTTGAAGGTATTACTTAACTTCACTAC AGATTGTCTAGAAGACCTTTCTAGGAGTTATCTGATTCTAGAAGGGTCTATACTTGTCCTTG TCTTTAAGCTATTTGACAACTCTACGTGTTGTAGAAAACTGATAATAATACAAATGATTGTT

245/310 FIGURE 242

MRSCLWRCRHLSQGVQWSLLLAVLVFFLFALPSFIKEPQTKPSRHQRTENIKERSLQSLAKP
KSQAPTRARRTTIYAEPAPENNALNTQTQPKAHTTGDRGKEANQAPPEEQDKVPHTAQRAAW
KSPEKEKTMVNTLSPRGQDAGMASGRTEAQSWKSQDTKTTQGNGGQTRKLTASRTVSEKHQG
KAATTAKTLIPKSQHRMLAPTGAVSTRTRQKGVTTAVIPPKEKKPQATPPPAPFQSPTTQRN
QRLKAANFKSEPRWDFEEKYSFEIGGLQTTCPDSVKIKASKSLWLQKLFLPNLTLFLDSRHF
NQSEWDRLEHFAPPFGFMELNYSLVQKVVTRFPPVPQQQLLLASLPAGSLRCITCAVVGNGG
ILNNSHMGQEIDSHDYVFRLSGALIKGYEQDVGTRTSFYGFTAFSLTQSLLILGNRGFKNVP
LGKDVRYLHFLEGTRDYEWLEALLMNQTVMSKNLFWFRHRPQEAFREALHMDRYLLLHPDFL
RYMKNRFLRSKTLDGAHWRIYRPTTGALLLLTALQLCDQVSAYGFITEGHERFSDHYYDTSW
KRLIFYINHDFKLEREVWKRLHDEGIIRLYQRPGPGTAKAKN

-248/310 FIGURE 244

 ${\tt MRGPGHPLLLGLLLVLGPSPEQRVEIVPRDLRMKDKFLKHLTGPLYFSPKCSKHFHRLYHNT} \\ {\tt RDCTIPAYYKRCARLLTRLAVSPVCMEDK}$

WO 99/63088

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GGGCTGGGCCCGCCGCAGCTCCAGCTGGCCGGCTTGGTCCTGCGGTCCCTTCTCTGGGAGG CCCGACCCCGGCCGCCCCACCCACCATGCCACCGCGGGGCTCCGCCGGGCCGCCCG CTCACCGCAATCGCTCTGTTGGTGCTGGGGGGCTCCCCTGGTGCTGGCCGGCGAGGACTGCCT GTGGTACCTGGACCGGAATGGCTCCTGGCATCCGGGGTTTAACTGCGAGTTCTTCACCTTCT GCTGCGGGACCTGCTACCATCGGTACTGCTGCAGGGACCTGACCTTGCTTATCACCGAGAGG CAGCAGAAGCACTGCCTGGCCTTCAGCCCCAAGACCATAGCAGGCATCGCCTCAGCTGTGAT CCTCTTTGTTGCTGTGGTTGCCACCACCATCTGCTGCTTCCTGTTCCTGTTGCTACCTGT ACCGCCGGCGCCAGCAGCTCCAGAGCCCATTTGAAGGCCAGGAGATTCCAATGACAGGCATC CCAGTGCAGCCAGTATACCCATACCCCCAGGACCCCAAAGCTGGCCCTGCACCCCCACAGCC TGGCTTCATGTACCCACCTAGTGGTCCTGCTCCCCAATATCCACTCTACCCAGCTGGGCCCC CAGTCTACAACCCTGCAGCTCCTCCCTATATGCCACCACAGCCCTCTTACCCGGGAGCC TGAGGAACCAGCCATGTCTCTGCTGCCCCTTCAGTGATGCCAACCTTGGGAGATGCCCTCAT CCTGTACCTGCATCTGGTCCTGGGGGTGGCAGGAGTCCTCCAGCCACCAGGCCCCAGACCAA GCCAAGCCCTGGGCCCTACTGGGGACAGAGCCCCCAGGGAAGTGGAACAGGAGCTGAACTAGA ACTATGAGGGGTTGGGGGGGGGGCTTGGAATTATGGGCTATTTTTACTGGGGGCAAGGGAGG GAGATGACAGCCTGGGTCACAGTGCCTGTTTTCAAATAGTCCCTCTGCTCCCAAGATCCCAG CCAGGAAGGCTGGGGCCCTACTGTTTGTCCCCTCTGGGCTGGGGTGGGGGGAGGAGGAGGT TCCGTCAGCAGCTGGCAGTAGCCCTCCTCTCTGGCTGCCCCACTGGCCACATCTCTGGCCTG CTAGATTAAAGCTGTAAAGACAAAA

そらり/310 FIGURE 246

MPPAGLRRAAPLTAIALLVLGAPLVLAGEDCLWYLDRNGSWHPGFNCEFFTFCCGTCYHRYC CRDLTLLITERQQKHCLAFSPKTIAGIASAVILFVAVVATTICCFLCSCCYLYRRRQQLQSP FEGQEIPMTGIPVQPVYPYPQDPKAGPAPPQPGFMYPPSGPAPQYPLYPAGPPVYNPAAPPP YMPPQPSYPGA

FIGURE 247

GGGGGAGCTAGGCCGGCGCAGTGGTGGTGGCGCCGCGCGCAAGGGTGAGGGCGCCCCAGAA CCCCAGGTAGGTAGAGCAAGAAGATGGTGTTTCTGCCCCTCAAATGGTCCCTTGCAACCATG TCATTTCTACTTTCCTCACTGTTGGCTCTCTTAACTGTGTCCACTCCTTCATGGTGTCAGAG CACTGAAGCATCTCCAAAACGTAGTGATGGGACACCATTTCCTTGGAATAAAATACGACTTC CTGAGTACGTCATCCCAGTTCATTATGATCTCTTGATCCATGCAAACCTTACCACGCTGACC TTCTGGGGAACCACGAAAGTAGAAATCACAGCCAGTCAGCCCACCAGCACCATCATCCTGCA TAGTCACCACCTGCAGATATCTAGGGCCACCCTCAGGAAGGGAGCTGGAGAGAGGCTATCGG AAGAACCCCTGCAGGTCCTGGAACACCCCCCTCAGGAGCAAATTGCACTGCTGGCTCCCGAG CCCCTCCTTGTCGGGCTCCCGTACACAGTTGTCATTCACTATGCTGGCAATCTTTCGGAGAC CAACACAATTTGAACCCACTGCAGCTAGAATGGCCTTTCCCTGCTTTGATGAACCTGCCTTC AAAGCAAGTTTCTCAATCAAAATTAGAAGAGAGCCAAGGCACCTAGCCATCTCCAATATGCC ATTGGTGAAATCTGTGACTGTTGCTGAAGGACTCATAGAAGACCATTTTGATGTCACTGTGA AGATGAGCACCTATCTGGTGGCCTTCATCATTTCAGATTTTGAGTCTGTCAGCAAGATAACC AAGAGTGGAGTCAAGGTTTCTGTTTATGCTGTGCCAGACAAGATAAATCAAGCAGATTATGC ACTGGATGCTGCGGTGACTCTTCTAGAATTTTATGAGGATTATTTCAGCATACCGTATCCCC TACCCAAACAAGATCTTGCTGCTATTCCCGACTTTCAGTCTGGTGCTATGGAAAACTGGGGA CTGACAACATATAGAGAATCTGCTCTGTTGTTTGATGCAGAAAAGTCTTCTGCATCAAGTAA GCTTGGCATCACAGTGACTGTGGCCCATGAACTGGCCCACCAGTGGTTTGGGAACCTGGTCA CTATGGAATGGTGGAATGATCTTTGGCTAAATGAAGGATTTGCCAAATTTATGGAGTTTGTG TCTGTCAGTGTGACCCATCCTGAACTGAAAGTTGGAGATTATTTCTTTGGCAAATGTTTTGA CGCAATGGAGGTAGATGCTTTAAATTCCTCACACCCTGTGTCTACACCTGTGGAAAATCCTG CTCAGATCCGGGAGATGTTTGATGATGTTTCTTATGATAAGGGAGCTTGTATTCTGAATATG CTAAGGGAGTATCTTAGCGCTGACGCATTTAAAAGTGGTATTGTACAGTATCTCCAGAAGCA TAGCTATAAAAATACAAAAAACGAGGACCTGTGGGATAGTATGGCAAGTATTTGCCCTACAG ATGGTGTAAAAGGGATGGATGGCTTTTGCTCTAGAAGTCAACATTCATCTTCATCCTCACAT TGGCATCAGGAAGGGGTGGATGTGAAAACCATGATGAACACTTGGACACTGCAGAGGGGTTT TCCCCTAATAACCATCACAGTGAGGGGGGGGGAATGTACACATGAAGCAAGAGCACTACATGA AGGGCTCTGACGGCGCCCCGGACACTGGGTACCTGTGGCATGTTCCATTGACATTCATCACC AGCAAATCCAACATGGTCCATCGATTTTTGCTAAAAACAAAAACAGATGTGCTCATCCTCCC AGAAGAGGTGGAATGGATCAAATTTAATGTGGGCATGAATGGCTATTACATTGTGCATTACG AATGATCGGGCAAGTCTCATTAACAATGCATTTCAGCTCGTCAGCATTGGGAAGCTGTCCAT TGAAAAGGCCTTGGATTTATCCCTGTACTTGAAACATGAAACTGAAATTATGCCCGTGTTTC GAAACTCAATTCAAGGCCTTCCTCATCAGGCTGCTAAGGGACCTCATTGATAAGCAGACATG GACAGACGAGGGCTCAGTCTCAGAGCAAATGCTGCGGAGTGAACTACTACTCCTCGCCTGTG AATGGAAACTTGAGCCTGCCTGTCGACGTGACCTTGGCAGTGTTTGCTGTGGGGGCCCAGAG CACAGAAGGCTGGGATTTTCTTTATAGTAAATATCAGTTTTCTTTGTCCAGTACTGAGAAAA GCCAAATTGAATTTGCCCTCTGCAGAACCCAAAATAAGGAAAAGCTTCAATGGCTACTAGAT GAAAGCTTTAAGGGAGATAAAATAAAAACTCAGGAGTTTCCACAAATTCTTACACTCATTGG CAGGAACCCAGTAGGATACCCACTGGCCTGGCAATTTCTGAGGAAAAACTGGAACAAACTTG TACAAAAGTTTGAACTTGGCTCATCTTCCATAGCCCACATGGTAATGGGTACAACAAATCAA TTCTCAGCTCCGTTGTGTCCAACAGACAATTGAAACCATTGAAGAAAACATCGGTTGGATGG ATAAGAATTTTGATAAAATCAGAGTGTGGCTGCAAAGTGAAAAGCTTGAACGTATG<u>TAA</u>AAA TTCCTCCCTTGCCCGGTTCCTGTTATCTCTAATCACCAACATTTTGTTGAGTGTATTTTCAA ACTAGAGATGGCTGTTTTGGCTCCAACTGGAGATACTTTTTTCCCTTCAACTCATTTTTTGA CTATCCCTGTGAAAAGAATAGCTGTTAGTTTTTCATGAATGGGCTTTTTCATGAATGGGCTA TCGCTACCATGTGTTTTGTTCATCACAGGTGTTGCCCTGCAACGTAAACCCCAAGTGTTGGGT

FIGURE 248

MVFLPLKWSLATMSFLLSSLLALLTVSTPSWCQSTEASPKRSDGTPFPWNKIRLPEYVIPVH YDLLIHANLTTLTFWGTTKVEITASQPTSTIILHSHHLQISRATLRKGAGERLSEEPLQVLE HPPQEQIALLAPEPLLVGLPYTVVIHYAGNLSETFHGFYKSTYRTKEGELRILASTQFEPTA ARMAFPCFDEPAFKASFSIKIRREPRHLAISNMPLVKSVTVAEGLIEDHFDVTVKMSTYLVA FIISDFESVSKITKSGVKVSVYAVPDKINQADYALDAAVTLLEFYEDYFSIPYPLPKQDLAA IPDFQSGAMENWGLTTYRESALLFDAEKSSASSKLGITVTVAHELAHQWFGNLVTMEWWNDL WLNEGFAKFMEFVSVSVTHPELKVGDYFFGKCFDAMEVDALNSSHPVSTPVENPAQIREMFD DVSYDKGACILNMLREYLSADAFKSGIVQYLQKHSYKNTKNEDLWDSMASICPTDGVKGMDG FCSRSQHSSSSSHWHQEGVDVKTMMNTWTLQRGFPLITITVRGRNVHMKQEHYMKGSDGAPD TGYLWHVPLTFITSKSNMVHRFLLKTKTDVLILPEEVEWIKFNVGMNGYYIVHYEDDGWDSL TGLLKGTHTAVSSNDRASLINNAFQLVSIGKLSIEKALDLSLYLKHETEIMPVFQGLNELIP MYKLMEKRDMNEVETQFKAFLIRLLRDLIDKQTWTDEGSVSEQMLRSELLLLACVHNYQPCV QRAEGYFRKWKESNGNLSLPVDVTLAVFAVGAQSTEGWDFLYSKYQFSLSSTEKSQIEFALC RTQNKEKLQWLLDESFKGDKIKTQEFPQILTLIGRNPVGYPLAWQFLRKNWNKLVQKFELGS SSIAHMVMGTTNQFSTRTRLEEVKGFFSSLKENGSQLRCVQQTIETIEENIGWMDKNFDKIR **VWLQSEKLERM**

WO 99/63088

258/310

FIGURE 249

 ${\tt CAGCCACAGACGGGTC\underline{ATGAGCGCGGTATTACTGCTGGCCCTCCTGGGGTTCATCCTCCCAC}}$ TGCCAGGAGTGCAGGCGCTGCTCTGCCAGTTTGGGACAGTTCAGCATGTGTGGAAGGTGTCC GACCTACCCCGGCAATGGACCCCTAAGAACACCAGCTGCGACAGCGGCTTGGGGTGCCAGGA CACGTTGATGCTCATTGAGAGCGGACCCCAAGTGAGCCTGGTGCTCTCCAAGGGCTGCACGG AGGCCAAGGACCAGGAGCCCCGCGTCACTGAGCACCGGATGGGCCCCGGCCTCTCCCTGATC TTGGGCCCCACAGCCCCCAGCAGACCCAGGATCCTTGAGGTGCCCAGTCTGCTTATGG AAGGCTGTCTGGAGGGGACAACAGAAGAGATCTGCCCCAAGGGGACCACACACTGTTATGAT CCAGCCAGGTTGCAACCTGCTCAATGGGACACAGGAAATTGGGCCCGTGGGTATGACTGAGA ACTGCAATAGGAAAGATTTTCTGACCTGTCATCGGGGGACCACCATTATGACACACGGAAAC TTGGCTCAAGAACCCACTGATTGGACCACATCGAATACCGAGATGTGCGAGGTGGGGCAGGT GTGTCAGGAGACGCTGCTCATAGATGTAGGACTCACATCAACCCTGGTGGGGACAAAAG GCTGCAGCACTGTTGGGGCTCAAAATTCCCAGAAGACCACCATCCACTCAGCCCCTCCTGGG GTGCTTGTGGCCTCCTATACCCACTTCTGCTCCTCGGACCTGTGCAATAGTGCCAGCAGCAG CAGCGTTCTGCTGAACTCCCTCCTCCTCAAGCTGCCCCTGTCCCAGGAGACCGGCAGTGTC CTACCTGTGTGCAGCCCCTTGGAACCTGTTCAAGTGGCTCCCCCCGAATGACCTGCCCCAGG GGCGCCACTCATTGTTATGATGGGTACATTCATCTCTCAGGAGGTGGGCTGTCCACCAAAAT GAGCATTCAGGGCTGCGTGGCCCAACCTTCCAGCTTCTTGTTGAACCACACCAGACAAATCG GGGGCTGAGGGCCTGGAGTCTCTCACTTGGGGGGTGGGGCTGGCACTGGCCCCAGCGCTGTG $\tt GTGGGGAGTGGTTTGCCCTTCCTGC\underline{TAA}CTCTATTACCCCCACGATTCTTCACCGCTGCTGA$ CCACCCACACTCAACCTCCCTCTGACCTCATAACCTAATGGCCTTGGACACCAGATTCTTTC ACACTGGGGAGAGCCTGGAGCATCCGGACTTGCCCTATGGGAGAGGGGACGCTGGAGGAGTG GCTGCATGTATCTGATAATACAGACCCTGTCCTTTCA

FIGURE 250

MSAVLLLALLGFILPLPGVQALLCQFGTVQHVWKVSDLPRQWTPKNTSCDSGLGCQDTLMLI
ESGPQVSLVLSKGCTEAKDQEPRVTEHRMGPGLSLISYTFVCRQEDFCNNLVNSLPLWAPQP
PADPGSLRCPVCLSMEGCLEGTTEEICPKGTTHCYDGLLRLRGGGIFSNLRVQGCMPQPGCN
LLNGTQEIGPVGMTENCNRKDFLTCHRGTTIMTHGNLAQEPTDWTTSNTEMCEVGQVCQETL
LLIDVGLTSTLVGTKGCSTVGAQNSQKTTIHSAPPGVLVASYTHFCSSDLCNSASSSSVLLN
SLPPQAAPVPGDRQCPTCVQPLGTCSSGSPRMTCPRGATHCYDGYIHLSGGGLSTKMSIQGC
VAQPSSFLLNHTRQIGIFSAREKRDVQPPASQHEGGGAEGLESLTWGVGLALAPALWWGVVCPSC

CAGGATGAGGGGGAATCTGGCCCTGGTGGGCGTTCTAATCAGCCTGGCCTTCCTGTCACTGCTG CCATCTGGACATCCTCAGCCGGCTGGCGATGACGCCTGCTCTGTGCAGATCCTCGTCCCTGG CCTCAAAGGGGATGCGGGAGAGAGGGGACAAAGGCGCCCCGGACGGCCTGGAAGAGTCG GCCCCACGGGAGAAAAAGGAGACATGGGGGACAAAGGACAGAAAGGCAGTGTGGGTCGTCAT GGAAAAATTGGTCCCATTGGCTCTAAAGGTGAGAAAGGAGATTCCGGTGACATAGGACCCCC AGATGGACAACCAGGTCTCTCAGCTGACCAGCGAGCTCAAGTTCATCAAGAATGCTGTCGCC GGTGTGCGCGAGACGGAGAGCAAGATCTACCTGCTGGTGAAGGAGGAGAAGCGCTACGCGGA CGCCCAGCTGTCCTGCCAGGGCCGCGGGGGCACGCTGAGCATGCCCAAGGACGAGGCTGCCA ATGGCCTGATGGCCGCATACCTGGCGCAAGCCGGCCTGGCCCGTGTCTTCATCGGCATCAAC GACCTGGAGAAGGAGGGCGCCTTCGTGTACTCTGACCACTCCCCCATGCGGACCTTCAACAA GTGGCGCAGCGGTGAGCCCAACAATGCCTACGACGAGGAGGACTGCGTGGAGATGGTGGCCT CGGGCGGCTGGAACGACGTGGCCTGCCACACCACCATGTACTTCATGTGTGAGTTTGACAAG GAGAACATGTGAGCCTCAGGCTGGGGCTGCCCATTGGGGGCCCCACATGTCCCTGCAGGGTT GGCAGGGACAGAGCCCAGACCATGGTGCCAGCCAGGGAGCTGTCCCTCTGTGAAGGGTGGAG GCTCACTGAGTAGAGGGCTGTTGTCTAAACTGAGAAAATGGCCTATGCTTAAGAGGAAAATG AAAGTGTTCCTGGGGTGCTGTCTCTGAAGAAGCAGAGTTTCATTACCTGTATTGTAGCCCCA ATGTCATTATGTAATTATTACCCAGAATTGCTCTTCCATAAAGCTTGTGCCTTTGTCCAAGC

FIGURE 252

MRGNLALVGVLISLAFLSLLPSGHPQPAGDDACSVQILVPGLKGDAGEKGDKGAPGRPGRVG
PTGEKGDMGDKGQKGSVGRHGKIGPIGSKGEKGDSGDIGPPGPNGEPGLPCECSQLRKAIGE
MDNQVSQLTSELKFIKNAVAGVRETESKIYLLVKEEKRYADAQLSCQGRGGTLSMPKDEAAN
GLMAAYLAQAGLARVFIGINDLEKEGAFVYSDHSPMRTFNKWRSGEPNNAYDEEDCVEMVAS
GGWNDVACHTTMYFMCEFDKENM

AGTGACTGCAGCCTTCCTAGATCCCCTCCACTCGGTTTCTCTCTTTGCAGGAGCACCGGCAG CACCAGTGTGTGAGGGGAGCAGGCAGCGGTCCTAGCCAGTTCCTTGATCCTGCCAGACCACC $\tt CAGCCCCGGCACAGAGCTGCTCCACAGGCACC\underline{ATG}AGGATCATGCTGCTATTCACAGCCAT$ TTCCTGGCGGGGGCCGCAGCAAGAGGGATCCAGATCTCTACCAGCTGCTCCAGAGACTCTTC AAAAGCCACTCATCTCTGGAGGGATTGCTCAAAGCCCTGAGCCAGGCTAGCACAGATCCTAA GGAATCAACATCTCCCGAGAAACGTGACATGCATGACTTCTTTGTGGGACTTATGGGCAAGA GGAGCGTCCAGCCAGAGGGAAAGACAGGACCTTTCTTACCTTCAGTGAGGGTTCCTCGGCCC CTTCATCCCAATCAGCTTGGATCCACAGGAAAGTCTTCCCTGGGAACAGAGGAGCAGAGACC TTTATAAGACTCTCCTACGGATGTGAATCAAGAGAACGTCCCCAGCTTTGGCATCCTCAAGT ATCCCCCGAGAGCAGAATAGGTACTCCACTTCCGGACTCCTGGACTGCATTAGGAAGACCTC AACATTCTTGTGCTTTGACTCCTTCTCCATCTTTTCTACCTGACCCTGGTGTGGAAACTGCA TAGTGAATATCCCCAACCCCAATGGGCATTGACTGTAGAATACCCTAGAGTTCCTGTAGTGT CCTACATTAAAAATATAATGTCTCTCTCTATTCCTCAACAATAAAGGATTTTTGCATATGAA *АААААААААААААААААААААААААААААААА*

FIGURE 254

MRIMLLFTAILAFSLAQSFGAVCKEPQEEVVPGGGRSKRDPDLYQLLQRLFKSHSSLEGLLK ALSQASTDPKESTSPEKRDMHDFFVGLMGKRSVQPEGKTGPFLPSVRVPRPLHPNQLGSTGK SSLGTEEQRPL

২59 / ১১০ FIGURE 255

GGGCGTCTCCGGCTGCTCCTATTGAGCTGTCTGCTCGCTGTGCCCGCTGTGCCTGTGCC CGCGCTGTCGCCGCTGCTACCGCGTCTGCTGGACGCGGGAGACGCCAGCCGAGCTGGTGATTG GAGCCCTGCGGAGAGCTCAAGCGCCCAGCTCTGCCCCAGGAGCCCAGGCTGCCCCGTGAGTC CCATAGTTGCTGCAGGAGTGGAGCCATGAGCTGCGTCCTGGGTGGTGTCATCCCCTTGGGGC TGCTGTTCCTGGTCTGCGGATCCCAAGGCTACCTCCTGCCCAACGTCACTCTCTTAGAGGAG CTGCTCAGCAAATACCAGCACAACGAGTCTCACTCCCGGGTCCGCAGAGCCATCCCCAGGGA GGACAAGGAGGAGATCCTCATGCTGCACAACAAGCTTCGGGGCCAGGTGCAGCCTCAGGCCT CCAACATGGAGTACATGGTGAGCGCCGGCTCCGGCCGCAGAGGCTGGCACCGGGGTGGGGC TTGAGACAGGGTCTCACTCTGCCACTGACGCTGGAGTGCAATGGCACAATCGTCATGCCCTG AAACCTTAGACTCCCGGGGTTAAGCGATCCTGCTTCAGCCTCCCAAGTAGCTGGAACTACAG GCATGCACCATGGTGCCCAGCTAGATTTTAAATATTTTGTGGAGATGGGGGTCTTGCTACGT TGCCCAGGCTGGTCTTGAACTCCTAGGCTCAAGCAATCCTCCTGCCTCAGCCTCTCAAAGTG CTAGGATTATAGGCATGAGTCACCCTGTCTGGCTCTGGCTCTGTTCTTAACATTCTGCCAAA ACAACACGTGGGTTCCCTGTGCAGAGCCTGCCTCGTTGCCTTCATGTCACTCTTGGTAGC TCCACTGGGAACACAGCTCTCAGCCTTTCCCACCTGGAGGCAGAGTGGGGAGGGGCCCAGGG CTGGGCTTTGCTGATGCTGATCTCAGCTGTGCCACACGCTAGCTGCACCACCCTGACTTCTC GTGAGATAAGTCGAGGCTGTGAAGGGCCCGGCACAGACTGACCTGCCTCCCCAACCCCTAGG CTTTGCTAACCGGGAAAGGAGCTAACGGTGACAGAAGACAGCCAAGGTCAACCCTCCCGGGT GATTGTGATGGGTGTTCCAGGTGTGGTTGGGCGATGCTGCTACTTGACCCCAAGCTCCAGTG TGGAAACTTCCTTCCTGGCTGGTTTTCCAGAACTACAGAGGAATGGACCACAGTCTTCCAGG GTCCCTCCTCGTCCACCAACCGGGAGCCTCCACCTTGGCCATCCGTCAGCTATGAATGGCTT TTTAAACAAACCACGTCCCAGCCTGGGTAACATGGTAAAGCCCCGTCTCTACAAAAAAATC CAAGTTAGCCGGGCATGGTGGTGCGCACCTGTAGTCCCAGCTGCAGTGGGACTGAGGTGGAG GTGGAGGTGGGGGGGGGGGCTGAGGAAGGAGGATCGCTTGAGCCTGGGAAGTCGAGGCTGC AGTGAGCTGAGATTGCACCACTGCACTCCAGCCTGGGTGACAGAGCAAGACCCTGTCTCAAAAA

 ${\tt MSCVLGGVIPLGLLFLVCGSQGYLLPNVTLLEELLSKYQHNESHSRVRRAIPREDKEEILML} \\ {\tt HNKLRGQVQPQASNMEYMVSAGSGRRGWHRGWGLGHQPALFPSQLCSPASACDGWLRVSSGR} \\ {\tt GGSRLCSVLFVCFETGSHSATDAGVQWHNRHALKP} \\ {\tt .}$

 ${\tt MGSGLPLVLLLTLLGSSHGTGPGMTLQLKLKESFLTNSSYESSFLELLEKLCLLLHLPSGTS} \\ {\tt VTLHHARSQHHVVCNT}$

264/310 FIGURE 260

MIGYYLILFLMWGSSTVFCVLLIFTIAEASFSVENECLVDLCLLRICYKLSGVPNQCRVPLP SDCSK

~ 65/310 FIGURE 261

GAGGATTTGCCACAGCAGCGGATAGAGCAGGAGAGCACCACCGGAGCCCTTGAGACATCCTT GAGAAGAGCCACAGCATAAGAGACTGCCCTGCTTGGTGTTTTTGCAGGATGATGGTGGCCCTT CGAGGAGCTTCTGCATTGCTGGTTCTGTTCCTTGCAGCTTTTCTGCCCCCCGCCGCAGTGTAC CCAGGACCCAGCCATGGTGCATTACATCTACCAGCGCTTTCGAGTCTTGGAGCAAGGGCTGG AAAAATGTACCCAAGCAACGAGGGCATACATTCAAGAATTCCAAGAGTTCTCAAAAAATATA TCTGTCATGCTGGGAAGATGTCAGACCTACACAAGTGAGTACAAGAGTGCAGTGGGTAACTT ACGAGTGCATCGTATCAGAGGACAAGACACTGGCAGAAATGTTGCTCCAAGAAGCTGAAGAA GAGAAAAAGATCCGGACTCTGCTGAATGCAAGCTGTGACAACATGCTGATGGGCATAAAGTC TTTGAAAATAGTGAAGAAGATGATGGACACACATGGCTCTTGGATGAAAGATGCTGTCTATA ACTCTCCAAAGGTGTACTTATTAATTGGATCCAGAAACAACACTGTTTGGGAATTTGCAAAC ATACGGGCATTCATGGAGGATAACACCAAGCCAGCTCCCCGGAAGCAAATCCTAACACTTTC CTGGCAGGGAACAGGCCAAGTGATCTACAAAGGTTTTCTATTTTTCATAACCAAGCAACTT CTAATGAGATAATCAAATATAACCTGCAGAAGAGGGACTGTGGAAGATCGAATGCTGCTCCCA GGAGGGGTAGGCCGAGCATTGGTTTACCAGCACTCCCCCTCAACTTACATTGACCTGGCTGT GGATGAGCATGGGCTCTGGGCCATCCACTCTGGGCCAGGCACCCATAGCCATTTGGTTCTCA CAAAGATTGAGCCGGGCACACTGGGAGTGGAGCATTCATGGGATACCCCATGCAGAAGCCAG GATGCTGAAGCCTCATTCCTCTTGTGTGGGGTTCTCTATGTGGTCTACAGTACTGGGGGCCA GGGCCCTCATCGCATCACCTGCATCTATGATCCACTGGGCACTATCAGTGAGGAGGACTTGC CCAACTTGTTCTTCCCCAAGAGACCAAGAAGTCACTCCATGATCCATTACAACCCCAGAGAT AAGCAGCTCTATGCCTGGAATGAAGGAAACCAGATCATTTACAAACTCCAGACAAAGAGAAAA GCTGCCTCTGAAG<u>TAA</u>TGCATTACAGCTGTGAGAAAGAGCACTGTGGCTTTGGCAGCTGTTC AGTGTGTAGAAGTGGAAATACGTATGCCTCCTTTCCCAAATGTCACTGCCTTAGGTATCTTC CAAGAGCTTAGATGAGAGCATATCATCAGGAAAGTTTCAACAATGTCCATTACTCCCCCAAA CCTCCTGGCTCTCAAGGATGACCACATTCTGATACAGCCTACTTCAAGCCTTTTGTTTTACT CCCTAATATTCACCACTGGCTTTTCTCTCCCCTGGCCTTTGCTGAAGCTCTTCCCTCTTTTT CAAATGTCTATTGATATTCTCCCATTTTCACTGCCCAACTAAAATACTATTAATATTTCTTT CTTTTCTTTTCTTTTTTTGAGACAAGGTCTCACTATGTTGCCCAGGCTGGTCTCAAACTCC AGAGCTCAAGAGATCCTCCTGCCTCAGCCTCCTAAGTACCTGGGATTACAGGCATGTGCCAC CACACCTGGCTTAAAATACTATTTCTTATTGAGGTTTAACCTCTATTTCCCCTAGCCCTGTC CTTCCACTAAGCTTGGTAGATGTAATAATAAAGTGAAAATATTAACATTTGAATATCGCTTT CCAGGTGTGGAGTGTTTGCACATCATTGAATTCTCGTTTCACCTTTGTGAAACATGCACAAG TCTTTACAGCTGTCATTCTAGAGTTTAGGTGAGTAACACAATTACAAAGTGAAAGATACAGC TAGAAAATACTACAAATCCCATAGTTTTTCCATTGCCCAAGGAAGCATCAAATACGTATGTT TGTTCACCTACTCTTATAGTCAATGCGTTCATCGTTTCAGCCTAAAAATAATAGTCTGTCCC TTTAGCCAGTTTTCATGTCTGCACAAGACCTTTCAATAGGCCTTTCAAATGATAATTCCTCC AGAAAACCAGTCTAAGGGTGAGGACCCCAACTCTAGCCTCCTCTTGTCTTGCTGTCCTCTGT

€66/210 FIGURE 262

MMVALRGASALLVLFLAAFLPPPQCTQDPAMVHYIYQRFRVLEQGLEKCTQATRAYIQEFQE
FSKNISVMLGRCQTYTSEYKSAVGNLALRVERAQREIDYIQYLREADECIVSEDKTLAEMLL
QEAEEEKKIRTLLNASCDNMLMGIKSLKIVKKMMDTHGSWMKDAVYNSPKVYLLIGSRNNTV
WEFANIRAFMEDNTKPAPRKQILTLSWQGTGQVIYKGFLFFHNQATSNEIIKYNLQKRTVED
RMLLPGGVGRALVYQHSPSTYIDLAVDEHGLWAIHSGPGTHSHLVLTKIEPGTLGVEHSWDT
PCRSQDAEASFLLCGVLYVVYSTGGQGPHRITCIYDPLGTISEEDLPNLFFPKRPRSHSMIH
YNPRDKQLYAWNEGNQIIYKLQTKRKLPLK

e 67/310

FIGURE 263

GGGCGCCCGCGTACTCACTAGCTGAGGTGGCAGTGGTTCCACCAACATGGAGCTCTCGCAGA TGTCGGAGCTCATGGGGCTGTCGGTGTTGCTTGGGCTGCTGGCCCTGATGGCGACGGCGCG AAATGGATTTCCACCTGACAAATCTTCGGGATCCAAGAAGCAGAAACAATATCAGCGGATTC GGAAGGAGAGCCTCAACAACACAACTTCACCCACCGCCTCCTGGCTGCAGCTCTGAAGAGC CACAGCGGGAACATATCTTGCATGGACTTTAGCAGCAATGGCAAATACCTGGCTACCTGTGC AGATGATCGCACCATCCGCATCTGGAGCACCAAGGACTTCCTGCAGCGAGAGCACCGCAGCA TGAGAGCCAACGTGGAGCTGGACCACGCCACCCTGGTGCGCTTCAGCCCTGACTGCAGAGCC TTCATCGTCTGGCTGGCCAACGGGGACACCCTCCGTGTCTTCAAGATGACCAAGCGGGAGGA TGGGGGCTACACCTTCACAGCCACCCCAGAGGACTTCCCTAAAAAGCACAAGGCGCCTGTCA TCGACATTGGCATTGCTAACACAGGGAAGTTTATCATGACTGCCTCCAGTGACACCACTGTC ACACGCTGCTGTATCTCCCTGTGGCAGATTTGTAGCCTCGTGTGGCTTCACCCCAGATGTGA AGGTTTGGAAGTCTGCTTTGGAAAGAAGGGGGGGTTCCAGGAGGTGGTGCGAGCCTTCGAA CTAAAGGGCCACTCCGCGGCTGTGCACTCGTTTGCTTTCTCCAACGACTCACGGAGGATGGC TTCTGTCTCCAAGGATGGTACATGGAAACTGTGGGACACAGATGTGGAATACAAGAAGAAGC CTGGCCCTCTCCCCCAACGCCCAGGTCTTGGCCTTGGCCAGTGGCAGTAGTATTCATCTCTA CAATACCCGGCGGGCGAGAAGGAGGAGTGCTTTGAGCGGGTCCATGGCGAGTGTATCGCCA ACTTGTCCTTTGACATCACTGGCCGCTTTCTGGCCTCCTGTGGGGACCGGGCGGTGCGGCTG TTTCACAACACTCCTGGCCACCGAGCCATGGTGGAGGAGATGCAGGGCCACCTGAAGCGGCC CTCCAACGAGAGCACCCGCCAGAGGCTGCAGCAGCAGCTGACCCAGGCCCAAGAGACCCTGA AGAGCCTGGGTGCCCTGAAGAAG<u>TGA</u>CTCTGGGAGGGCCCGGCGCAGAGGATTGAGGAGGAG GGATCTGGCCTCCTCATGGCACTGCTGCCATCTTTCCTCCCAGGTGGAAGCCTTTCAGAAGG AGTCTCCTGGTTTTCTTACTGGTGGCCCTGCTTCTTCCCATTGAAACTACTCTTGTCTACTT AGGTCTCTCTCTTGCTGGCTGTGACTCCTCCCTGACTAGTGGCCAAGGTGCTTTTCTTC CTCCCAGGCCCAGTGGGTGGAATCTGTCCCCACCTGGCACTGAGGAGAATGGTAGAGAGGAG AGGAGAGAGAGAGAATGTGATTTTTGGCCTTGTGGCAGCACATCCTCACACCCAAAGAAG TTTGTAAATGTTCCAGAACAACCTAGAGAACACCTGAGTACTAAGCAGCAGTTTTGCAAGGA TGGGAGACTGGGATAGCTTCCCATCACAGAACTGTGTTCCATCAAAAAGACACTAAGGGATT TCCTTCTGGGCCTCAGTTCTATTTGTAAGATGGAGAATAATCCTCTCTGTGAACTCCTTGCA AAGATGATATGAGGCTAAGAGAATATCAAGTCCCCAGGTCTGGAAGAAAAGTAGAAAAAGAGT **AGTACTATTGTCCAATGTCATGAAAGTGGTAAAAGTGGGAACCAGTGTGCTTTGAAACCAAA** TTAGAAACACATTCCTTGGGAAGGCAAAGTTTTCTGGGACTTGATCATACATTTTATATGGT TGGGACTTCTCTCTCGGGAGATGATATCTTGTTTAAGGAGACCTCTTTTCAGTTCATCAAG

€ 68 /310 FIGURE 264

MELSQMSELMGLSVLLGLLALMATAAVARGWLRAGEERSGRPACQKANGFPPDKSSGSKKQK
QYQRIRKEKPQQHNFTHRLLAAALKSHSGNISCMDFSSNGKYLATCADDRTIRIWSTKDFLQ
REHRSMRANVELDHATLVRFSPDCRAFIVWLANGDTLRVFKMTKREDGGYTFTATPEDFPKK
HKAPVIDIGIANTGKFIMTASSDTTVLIWSLKGQVLSTINTNQMNNTHAAVSPCGRFVASCG
FTPDVKVWEVCFGKKGEFQEVVRAFELKGHSAAVHSFAFSNDSRRMASVSKDGTWKLWDTDV
EYKKKQDPYLLKTGRFEEAAGAAPCRLALSPNAQVLALASGSSIHLYNTRRGEKEECFERVH
GECIANLSFDITGRFLASCGDRAVRLFHNTPGHRAMVEEMQGHLKRASNESTRQRLQQQLTQ
AQETLKSLGALKK

TGGCCTCCCCAGCTTGCCAGGCACAAGGCTGAGCGGAGGAAGCGAGAGGCATCTAAGCAGG CAGTGTTTTGCCTTCACCCCAAGTGACC<u>ATG</u>AGAGGTGCCACGCGAGTCTCAATCATGCTCC TCCTAGTAACTGTGTCTGACTGTGCTGTGATCACAGGGGCCTGTGAGCGGGATGTCCAGTGT GGGGCAGGCACCTGCTGTGCCATCAGCCTGTGGCTTCGAGGGCTGCGGATGTGCACCCCGCT GGGGCGGGAAGGCGAGGAGTGCCACCCCGGCAGCCACAAGGTCCCCTTCTTCAGGAAACGCA AGCACCACACCTGTCCTTGCCTGCCCAACCTGCTGCTCCAGGTTCCCGGACGCAGGTAC CGCTGCTCCATGGACTTGAAGAACATCAATTTT<u>TAG</u>GCGCTTGCCTGGTCTCAGGATACCCA CCATCCTTTTCCTGAGCACAGCCTGGATTTTTATTTCTGCCATGAAACCCAGCTCCCATGAC TCTCCCAGTCCCTACACTGACTACCCTGATCTCTCTTGTCTAGTACGCACATATGCACACAG GCAGACATACCTCCCATCATGACATGGTCCCCAGGCTGGCCTGAGGATGTCACAGCTTGAGG CTGTGGTGTGAAAGGTGGCCAGCCTGGTTCTCTCTCCCTGCTCAGGCTGCCAGAGAGGTGGTA **AATGGCAGAAAGGACATTCCCCCTCCCCTCCCCAGGTGACCTGCTCTCTTTCCTGGGCCCTG** CCCCTCTCCCCACATGTATCCCTCGGTCTGAATTAGACATTCCTGGGCACAGGCTCTTGGGT GCATTGCTCAGAGTCCCAGGTCCTGGCCTGACCCTCAGGCCCTTCACGTGAGGTCTGTGAGG ACCAATTTGTGGGTAGTTCATCTTCCCTCGATTGGTTAACTCCTTAGTTTCAGACCACAGAC TCAAGATTGGCTCTTCCCAGAGGCAGCAGACAGTCACCCCAAGGCAGGTGTAGGGAGCCCA GGGAGGCCAATCAGCCCCTGAAGACTCTGGTCCCAGTCAGCCTGTGGCTTGTGGCCTGTGA CCTGTGACCTTCTGCCAGAATTGTCATGCCTCTGAGGCCCCCTCTTACCACACTTTACCAGT TAACCACTGAAGCCCCCAATTCCCACAGCTTTTCCATTAAAATGCAAATGGTGGTGGTTCAA TCTAATCTGATATTGACATATTAGAAGGCAATTAGGGTGTTTCCTTAAACAACTCCTTTCCA AGGATCAGCCCTGAGAGCAGGTTGGTGACTTTGAGGAGGGCAGTCCTCTGTCCAGATTGGGG TGGGAGCAAGGGACAGGGAGCAGGGCAGGGGCTGAAAGGGGCACTGATTCAGACCAGGGAGG CAACTACACCACCAACATGCTGGCTTTAGAATAAAAGCACCAACTGAAAAAA

~70/310 FIGURE 266

 ${\tt MRGATRVSIMLLLVTVSDCAVITGACERDVQCGAGTCCAISLWLRGLRMCTPLGREGEECHP} \\ {\tt GSHKVPFFRKRKHHTCPCLPNLLCSRFPDGRYRCSMDLKNINF}$

ح×1/310

AGCGCCCGGGCGTCGGGGCGTAAAAGGCCGGCAGAAGGGAGGCACTTGAGAAATGTCTTTC CTCCAGGACCCAAGTTTCTTCACCATGGGGATGTGGTCCATTGGTGCAGGAGCCCTGGGGGC TGCTGCCTTGGCATTGCTGCTTGCCAACACAGACGTGTTTCTGTCCAAGCCCCAGAAAGCGG CCCTGGAGTACCTGGAGGATATAGACCTGAAAACACTGGAGAAGGAACCAAGGACTTTCAAA GCAAAGGAGCTATGGGAAAAAAATGGAGCTGTGATTATGGCCGTGCGGAGGCCAGGCTGTTT CCTCTGTCGAGAGGAAGCTGCGGATCTGTCCTCCCTGAAAAGCATGTTGGACCAGCTGGGCG TCCCCCTCTATGCAGTGGTAAAGGAGCACATCAGGACTGAAGTGAAGGATTTCCAGCCTTAT TTCAAAGGAGAAATCTTCCTGGATGAAAAGAAAAGTTCTATGGTCCACAAAGGCGGAAGAT GATGTTTATGGGATTTATCCGTCTGGGAGTGTGGTACAACTTCTTCCGAGCCTGGAACGGAG GCTTCTCTGGAAACCTGGAAGGAGAAGGCTTCATCCTTGGGGGAGTTTTCGTGGTGGGATCA GGAAAGCAGGGCATTCTTCTTGAGCACCGAGAAAAAGAATTTGGAGACAAAGTAAACCTACT TTCTGTTCTGGAAGCTGCTAAGATGATCAAACCACAGACTTTGGCCTCAGAGAAAAAA<u>TGA</u>T TGTGTGAAACTGCCCAGCTCAGGGATAACCAGGGACATTCACCTGTGTTCATGGGATGTATT GTTTCCACTCGTGTCCCTAAGGAGTGAGAAACCCATTTATACTCTACTCTCAGTATGGATTA TTAATGTATTTTAATATTCTGTTTAGGCCCACTAAGGCAAAATAGCCCCAAAACAAGACTGA CAAAAATCTGAAAAACTAATGAGGATTATTAAGCTAAAACCTGGGAAATAGGAGGCTTAAAA TTGACTGCCAGGCTGGGTGCAGTGGCTCACACCTGTAATCCCAGCACTTTGGGAGGCCAAGG TGAGCAAGTCACTTGAGGTCGGGAGTTCGAGACCAGCCTGAGCAACATGGCGAAACCCCGTC GGAGGCTGAGGCAGGAGATCACTTGAACCTGGGAGGTGGAGGTTGCGGTGAGCTGAGATCA

MSFLQDPSFFTMGMWSIGAGALGAAALALLLANTDVFLSKPQKAALEYLEDIDLKTLEKEPR TFKAKELWEKNGAVIMAVRRPGCFLCREEAADLSSLKSMLDQLGVPLYAVVKEHIRTEVKDF QPYFKGEIFLDEKKKFYGPQRRKMMFMGFIRLGVWYNFFRAWNGGFSGNLEGEGFILGGVFV VGSGKQGILLEHREKEFGDKVNLLSVLEAAKMIKPQTLASEKK

MANPGLGLLLALGLPFLLARWGRAWGQIQTTSANENSTVLPSSTSSSSDGNLRPEAITAIIV VFSLLAALLLAVGLALLVRKLREKRQTEGTYRPSSEEQFSHAAEARAPQDSKETVQGCLPI

-2₹**5** /310 FIGURE 271

 ${\tt MTFFLSLLLLLVCEAIWRSNSGSNTLENGYFLSRNKENHSQPTQSSLEDSVTPTKAVKTTGK} \\ {\tt GIVKGRNLDSRGLILGAEAWGRGVKKNT}$

247/310

FIGURE 273

GCCAGGAATAACTAGAGAGGAACA<u>ATG</u>GGGTTATTCAGAGGTTTTGTTTTCCTCTTAGTTCT GTGCCTGCTGCACCAGTCAAATACTTCCTTCATTAAGCTGAATAATAATGGCTTTGAAGATA TTGTCATTGTTATAGATCCTAGTGTGCCAGAAGATGAAAAAATAATTGAACAAATAGAGGAT ATGGTGACTACAGCTTCTACGTACCTGTTTGAAGCCACAGAAAAAAGATTTTTTTCAAAAA TGTATCTATATTAATTCCTGAGAATTGGAAGGAAAATCCTCAGTACAAAAGGCCAAAACATG AAAACCATAAACATGCTGATGTTATAGTTGCACCACCTACACTCCCAGGTAGAGATGAACCA TACACCAAGCAGTTCACAGAATGTGGAGAGAAAGGCGAATACATTCACTTCACCCCTGACCT TCTACTTGGAAAAAACAAAATGAATATGGACCACCAGGCAAACTGTTTGTCCATGAGTGGG CTCACCTCCGGTGGGGAGTGTTTGATGAGTACAATGAAGATCAGCCTTTCTACCGTGCTAAG TCAAAAAAATCGAAGCAACAAGGTGTTCCGCAGGTATCTCTGGTAGAAATAGAGTTTATAA GTGTCAAGGAGGCAGCTGTCTTAGTAGAGCATGCAGAATTGATTCTACAACAAAACTGTATG GAAAAGATTGTCAATTCTTTCCTGATAAAGTACAAACAGAAAAAGCATCCATAATGTTTATG CAAAGTATTGATTCTGTTGTTGAATTTTGTAACGAAAAAACCCATAATCAAGAAGCTCCAAG CCTACAAAACATAAAGTGCAATTTTAGAAGTACATGGGAGGTGATTAGCAATTCTGAGGATT TTAAAAACACCATACCCATGGTGACACCACCTCCTCCACCTGTCTTCTCATTGCTGAAGATC AGTCAAAGAATTGTGTGCTTAGTTCTTGATAAGTCTGGAAGCATGGGGGGTAAGGACCGCCT **AAATCGAATGAATCAAGCAGCAAAACATTTCCTGCTGCAGACTGTTGAAAATGGATCCTGGG** TGGGGATGGTTCACTTTGATAGTACTGCCACTATTGTAAATAAGCTAATCCAAATAAAAAGC AGTGATGAAAGAAACACACTCATGGCAGGATTACCTACATATCCTCTGGGAGGAACTTCCAT CTGCTCTGGAATTAAATATGCATTTCAGGTGATTGGAGAGCTACATTCCCAACTCGATGGAT CCGAAGTACTGCTGACTGATGGGGAGGATAACACTGCAAGTTCTTGTATTGATGAAGTG AAACAAAGTGGGGCCATTGTTCATTTTATTGCTTTGGGAAGAGCTGCTGATGAAGCAGTAAT AGAGATGAGCAAGATAACAGGAGGAAGTCATTTTTATGTTTCAGATGAAGCTCAGAACAATG GCCTCATTGATGCTTTTGGGGCTCTTACATCAGGAAATACTGATCTCTCCCAGAAGTCCCTT CAGCTCGAAAGTAAGGGATTAACACTGAATAGTAATGCCTGGATGAACGACACTGTCATAAT TGATAGTACAGTGGGAAAGGACACGTTCTTTCTCATCACATGGAACAGTCTGCCTCCCAGTA TTTCTCTCTGGGATCCCAGTGGAACAATAATGGAAAATTTCACAGTGGATGCAACTTCCAAA ATGGCCTATCTCAGTATTCCAGGAACTGCAAAGGTGGGCACTTGGGCATACAATCTTCAAGC CAAAGCGAACCCAGAAACATTAACTATTACAGTAACTTCTCGAGCAGCAAATTCTTCTGTGC CTCCAATCACAGTGAATGCTAAAATGAATAAGGACGTAAACAGTTTCCCCAGCCCAATGATT GTTTACGCAGAAATTCTACAAGGATATGTACCTGTTCTTGGAGCCAATGTGACTGCTTTCAT TGAATCACAGAATGGACATACAGAAGTTTTGGAACTTTTGGATAATGGTGCAGGCGCTGATT CTTTCAAGAATGATGGAGTCTACTCCAGGTATTTTACAGCATATACAGAAAATGGCAGATAT AGCTTAAAAGTTCGGGCTCATGGAGGAGCAAACACTGCCAGGCTAAAATTACGGCCTCCACT GAATAGAGCCGCGTACATACCAGGCTGGGTAGTGAACGGGGAAATTGAAGCAAACCCGCCAA GACCTGAAATTGATGAGGATACTCAGACCACCTTGGAGGATTTCAGCCGAACAGCATCCGGA GGTGCATTTGTGGTATCACAAGTCCCAAGCCTTCCCTTGCCTGACCAATACCCACCAAGTCA AATCACAGACCTTGATGCCACAGTTCATGAGGATAAGATTATTCTTACATGGACAGCACCAG GAGATAATTTTGATGTTGGAAAAGTTCAACGTTATATCATAAGAATAAGTGCAAGTATTCTT GATCTAAGAGACAGTTTTGATGATGCTCTTCAAGTAAATACTACTGATCTGTCACCAAAGGA GGCCAACTCCAAGGAAAGCTTTGCATTTAAACCAGAAAATATCTCAGAAGAAAATGCAACCC ACATATTTATTGCCATTAAAAGTATAGATAAAAGCAATTTGACATCAAAAGTATCCAACATT GCACAAGTAACTTTGTTTATCCCTCAAGCAAATCCTGATGACATTGATCCTACACCTACTCC TACTCCTACTCCTACTCCTGATAAAAGTCATAATTCTGGAGTTAATATTTCTACGCTGGTAT TGTCTGTGATTGGGTCTGTTGTAATTGTTAACTTTATTTTAAGTACCACCATT<u>TGA</u>ACCTTA AAAGGATATTTCTGAATCTTAAAATTCATCCCATGTGTGATCATAAACTCATAAAAATAATT TTAAGATGTCGGAAAAGGATACTTTGATTAAATAAAAACACTCATGGATATGTAAAAACTGT AAAGATCCTTTTTCATACTGATACCTGGTTGTATATTATTTGATGCAACAGTTTTCTGAAAT **ААААААААААААААААААААААААААААААА**

マギ8/310 FIGURE 274

MGLFRGFVFLLVLCLLHQSNTSFIKLNNNGFEDIVIVIDPSVPEDEKIIEQIEDMVTTASTY
LFEATEKRFFFKNVSILIPENWKENPQYKRPKHENHKHADVIVAPPTLPGRDEPYTKQFTEC
GEKGEYIHFTPDLLLGKKQNEYGPPGKLFVHEWAHLRWGVFDEYNEDQPFYRAKSKKIEATR
CSAGISGRNRVYKCQGGSCLSRACRIDSTTKLYGKDCQFFPDKVQTEKASIMFMQSIDSVVE
FCNEKTHNQEAPSLQNIKCNFRSTWEVISNSEDFKNTIPMVTPPPPPVFSLLKISQRIVCLV
LDKSGSMGGKDRLNRMNQAAKHFLLQTVENGSWVGMVHFDSTATIVNKLIQIKSSDERNTLM
AGLPTYPLGGTSICSGIKYAFQVIGELHSQLDGSEVLLLTDGEDNTASSCIDEVKQSGAIVH
FIALGRAADEAVIEMSKITGGSHFYVSDEAQNNGLIDAFGALTSGNTDLSQKSLQLESKGLT
LNSNAWMNDTVIIDSTVGKDTFFLITWNSLPPSISLWDPSGTIMENFTVDATSKMAYLSIPG
TAKVGTWAYNLQAKANPETLTITVTSRAANSSVPPITVNAKMNKDVNSFPSPMIVYAEILQG
YVPVLGANVTAFIESQNGHTEVLELLDNGAGADSFKNDGVYSRYFTAYTENGRYSLKVRAHG
GANTARLKLRPPLNRAAYIPGWVVNGEIEANPPRPEIDEDTQTTLEDFSRTASGGAFVVSQV
PSLPLPDQYPPSQITDLDATVHEDKIILTWTAPGDNFDVGKVQRYIIRISASILDLRDSFDD
ALQVNTTDLSPKEANSKESFAFKPENISEENATHIFIAIKSIDKSNLTSKVSNIAQVTLFIP

セギ3/3×0 FIGURE 275

CTCCTTAGGTGGAAACCCTGGGAGTAGAGTACTGACAGCAAAGACCGGGAAAGACCATACGTCCCCGG GCAGGGGTGACAACAGGTGTCATCTTTTTGATCTCGTGTGTGGCTGCCTTCCTATTTCAAGGAAAGAC GCCAAGGTAATTTTGACCCAGAGGAGCAATGATGTAGCCACCTCCTAACCTTCCCTTCTTGAACCCCC AGTTATGCCAGGATTTACTAGAGAGTGTCAACTCAACCAGCAAGCGGCTCCTTCGGCTTAACTTGTGG TTGGAGGAGAACCTTTGTGGGGCTGCGTTCTCTTAGCAGTGCTCAGAAGTGACTTGCCTGAGGGTG GACCAGAAGAAGGAAAGGTCCCCTCTTGCTGTTGGCTGCACATCAGGAAGGCTGTGATGGGAATGAA AGCTGCTCTGTGTGGTGGTTAACTCCAAGAGGCAGAACTCGTTCTAGAAGGAAATGGATGCAAGCAGC TCCGGGGGCCCCAAACGCATGCTTCCTGTGGTCTAGCCCAGGGAAGCCCTTCCGTGGGGGCCCCGGCT ${\tt TTGAGGGATGCCACCGGTTCTGGACGCATGGCTGATTCCTGA} \underline{{\tt ATG}} \\ {\tt ATG} \underline{{\tt ATG}} \underline{{\tt AT$ TGCGTGGATTTCCCGGGTGGTGGTTTTGCTGGTGCTCCTCTGCTGCTATCTCTGTCCTGTACATGT TGGCCTGCACCCCAAAAGGTGACGAGGAGCAGCTGGCACTGCCCAGGGCCAACAGCCCCACGGGGAAG GAGGGGTACCAGGCCGTCCTTCAGGAGTGGGAGGAGCAGCACCGCAACTACGTGAGCAGCCTGAAGCG GCAGATCGCACAGCTCAAGGAGGAGCTGCAGGAGGAGGAGTGAGCAGCTCAGGAATGGGCAGTACCAAG CCAGCGATGCTGCCTGGGCCTGGGCCAGGAGAAAACCCAGGCCGACCTCCTGGCC TTCCTGCACTCGCAGGTGGACAAGGCAGAGGTGAATGCTGGCGTCAAGCTGGCCACAGAGTATGCAGC AGTGCCTTTCGATAGCTTTACTCTACAGAAGGTGTACCAGCTGGAGACTGGCCTTACCCGCCACCCCG AGGAGAAGCCTGTGAGGAAGGACAAGCGGGATGAGTTGGTGGAAGCCATTGAATCAGCCTTGGAGACC CTGAACAATCCTGCAGAGAACAGCCCCAATCACCGTCCTTACACGGCCTCTGATTTCATAGAAGGGAT CTACCGAACAGAAAGGGACAAAGGGACATTGTATGAGCTCACCTTCAAAGGGGACCACAAACACGAAT TCAAACGGCTCATCTTATTTCGACCATTCAGCCCCATCATGAAAGTGAAAAATGAAAAGCTCAACATG GCCAACACGCTTATCAATGTTATCGTGCCTCTAGCAAAAAGGGTGGACAAGTTCCGGCAGTTCATGCA GAATTTCAGGGAGATGTGCATTGAGCAGGATGGGAGAGTCCATCTCACTGTTGTTTACTTTGGGAAAG AAGAAATAAATGAAGTCAAAGGAATACTTGAAAACACTTCCAAAGCTGCCAACTTCAGGAACTTTACC TTCATCCAGCTGAATGGAGAATTTTCTCGGGGAAAGGGACTTGATGTTGGAGCCCGCTTCTGGAAGGG AAGCAACGTCCTTCTCTTTTTCTGTGATGTGGACATCTACTTCACATCTGAATTCCTCAATACGTGTA ATATACGGCCACCATGATGCAGTCCCTCCCTTGGAACAGCAGCTGGTCATAAAGAAGGAAACTGGATT TTGGAGAGACTTTGGATTTGGGATGACGTGTCAGTATCGGTCAGACTTCATCAATATAGGTGGGTTTG ATCTGGACATCAAAGGCTGGGGCGGAGAGGATGTGCACCTTTATCGCAAGTATCTCCACAGCAACCTC ATAGTGGTACGGACGCCTGTGCGAGGACTCTTCCACCTCTGGCATGAGAAGCGCTGCATGGACGAGCT GACCCCGAGCAGTACAAGATGTGCATGCAGTCCAAGGCCATGAACGAGGCATCCCACGGCCAGCTGG GCATGCTGGTGTTCAGGCACGAGATAGAGGCTCACCTTCGCAAACAGAAACAGAAGACAAGTAGCAAA GCTGCAACAGAGAAAAGACTTCCATAAAGGACGACAAAAGAATTGGACTGATGGGTCAGAGATGAGAA AGCCTCCGATTTCTCTCTGTTGGGCTTTTTACAACAGAAATCAAAAATCTCCGCTTTGCCTGCAAAAGT AACCCAGTTGCACCCTGTGAAGTGTCTGACAAAGGCAGAATGCTTGTGAGATTATAAGCCTAATGGTG TGGAGGTTTTGATGGTGTTTACAATACACTGAGACCTGTTGTTTTGTGTGCTCATTGAAATATTCATG TTATGATACTAGTGAGTACATTAAGTAAAATAAAATGGACCAGAAAAGAAAAGAAACCATAAATATCG TGTCATATTTTCCCCAAGATTAACCAAAAATAATCTGCTTATCTTTTTGGTTGTCCTTTTAACTGTCT CCGTTTTTTTCTTTTATTTAAAAATGCACTTTTTTTCCCTTGTGAGTTATAGTCTGCTTATTTAATTA CCACTTTGCAAGCCTTACAAGAGAGCACAAGTTGGCCTACATTTTTATATTTTTTAAGAAGATACTTT GAGATGCATTATGAGAACTTTCAGTTCAAAGCATCAAATTGATGCCATATCCAAGGACATGCCAAATG CGTACAGATACTTTCTCTGAAGAGTATTTTCGAAGAGGAGCAACTGAACACTGGAGGAAAAGAAAATG ACACTTTCTGCTTTACAGAAAAGGAAACTCATTCAGACTGGTGATATCGTGATGTACCTAAAAGTCAG GTGAACCAAACAATCTCTTTTCAAAACAGGGTGCTCCTCCTGGCTTCTGGCTTCCATAAGAAGAAAATG GAGAAAAATATATATATATATATATATTGTGAAAGATCAATCCATCTGCCAGAATCTAGTGGGATG GAAGTTTTTGCTACATGTTATCCACCCCAGGCCAGGTGGAAGTAACTGAATTATTTTTTAAATTAAGC AGTTCTACTCAATCACCAAGATGCTTCTGAAAATTGCATTTTATTACCATTTCAAACTATTTTTTAAA AATAAATACAGTTAACATAGAGTGGTTTCTTCATTCATGTGAAAATTATTAGCCAGCACCAGATGCAT GAGCTAATTATCTCTTTGAGTCCTTGCTTCTGTTTGCTCACAGTAAACTCATTGTTTAAAAGCTTCAA GAACATTCAAGCTGTTGGTGTTTAAAAAATGCATTGTATTGATTTGTACTGGTAGTTTATGAAATTT AATTAAAACACAGGCCATGAATGGAAGGTGGTATTGCACAGCTAATAAAATATGATTTGTGGATATGAA

≈8°/3\0 FIGURE 276

MMMVRRGLLAWISRVVVLLVLLCCAISVLYMLACTPKGDEEQLALPRANSPTGKEGYQAVLQ
EWEEQHRNYVSSLKRQIAQLKEELQERSEQLRNGQYQASDAAGLGLDRSPPEKTQADLLAFL
HSQVDKAEVNAGVKLATEYAAVPFDSFTLQKVYQLETGLTRHPEEKPVRKDKRDELVEAIES
ALETLNNPAENSPNHRPYTASDFIEGIYRTERDKGTLYELTFKGDHKHEFKRLILFRPFSPI
MKVKNEKLNMANTLINVIVPLAKRVDKFRQFMQNFREMCIEQDGRVHLTVVYFGKEEINEVK
GILENTSKAANFRNFTFIQLNGEFSRGKGLDVGARFWKGSNVLLFFCDVDIYFTSEFLNTCR
LNTQPGKKVFYPVLFSQYNPGIIYGHHDAVPPLEQQLVIKKETGFWRDFGFGMTCQYRSDFI
NIGGFDLDIKGWGGEDVHLYRKYLHSNLIVVRTPVRGLFHLWHEKRCMDELTPEQYKMCMQS
KAMNEASHGQLGMLVFRHEIEAHLRKQKQKTSSKKT

-081/310

FIGURE 277

 ${\tt GAAAGAATG}$ TTGTGGCTGCTCTTTTTCTGGTGACTGCCATTCATGCTGAACTCTGTCAACC AGGTGCAGAAAATGCTTTTAAAGTGAGACTTAGTATCAGAACAGCTCTGGGAGATAAAGCAT ATGCCTGGGATACCAATGAAGAATACCTCTTCAAAGCGATGGTAGCTTTCTCCATGAGAAAA GTTCCCAACAGAGAAGCAACAGAAATTTCCCATGTCCTACTTTGCAATGTAACCCAGAGGGT ATCATTCTGGTTTGTGGTTACAGACCCTTCAAAAAATCACACCCTTCCTGCTGTTGAGGTGC CTGGAATTTTTAAAAATCCCTTCCACACTTGCACCACCCATGGACCCATCTGTGCCCATCTG GATTATTATATTTGGTGTGATATTTTGCATCATCATAGTTGCAATTGCACTACTGATTTTAT CAGGGATCTGGCAACGTAGAAGAAGAACAAAGAACCATCTGAAGTGGATGACGCTGAAGAT AAGTGTGAAAACATGATCACAATTGAAAATGGCATCCCCTCTGATCCCCTGGACATGAAGGG $GGGCATATTAATGATGCCTTCA\underline{TGA}CAGAGGATGAGAGGCTCACCCCTCTCTGAAGGGCTGT$ TGTTCTGCTTCCTCAAGAAATTAAACATTTGTTTCTGTGTGACTGCTGAGCATCCTGAAATA CCAAGAGCAGATCATATATTTTGTTTCACCATTCTTCTTTTGTAATAAATTTTGAATGTGCT TGAAAGTGAAAAGCAATCAATTATACCCACCAACACCACTGAAATCATAAGCTATTCACGAC TCAAAATATTCTAAAATATTTTTCTGACAGTATAGTGTATAAATGTGGTCATGTGGTATTTG TAGTTATTGATTTAAGCATTTTTAGAAATAAGATCAGGCATATGTATATATTTTCACACTTC AAAGACCTAAGGAAAAATAAATTTTCCAGTGGAGAATACATATAATATGGTGTAGAAATCAT TGAAAATGGATCCTTTTTGACGATCACTTATATCACTCTGTATATGACTAAGTAAACAAAAG TGAGAAGTAATTATTGTAAATGGATGGATAAAAATGGAATTACTCATATACAGGGTGGAATT TTATCCTGTTATCACACCAACAGTTGATTATATATTTTCTGAATATCAGCCCCTAATAGGAC AATTCTATTTGTTGACCATTTCTACAATTTGTAAAAGTCCAATCTGTGCTAACTTAATAAAG

MLWLLFFLVTAIHAELCQPGAENAFKVRLSIRTALGDKAYAWDTNEEYLFKAMVAFSMRKVP NREATEISHVLLCNVTQRVSFWFVVTDPSKNHTLPAVEVQSAIRMNKNRINNAFFLNDQTLE FLKIPSTLAPPMDPSVPIWIIIFGVIFCIIIVAIALLILSGIWQRRKNKEPSEVDDAEDKC ENMITIENGIPSDPLDMKGGILMMPS

WO 99/63088

FIGURE 279

AACTCAAACTCCTCTCTCTGGGAAAACGCGGTGCTTGCTCCTCCCGGAGTGGCCTTGGCAGG ATGGCAAGAGCTCTACTCGTGCGGTGCTTCTTCTCCTTGGCATACAGCTCACAGCTCTTTGG CCTATAGCAGCTGTGGAAATTTATACCTCCCGGGTGCTGGAGGCTGTTAATGGGACAGATGC TCGGTTAAAATGCACTTTCTCCAGCTTTGCCCCTGTGGGTGATGCTCTAACAGTGACCTGGA ATTTTCGTCCTCTAGACGGGGACCTGAGCAGTTTGTATTCTACTACCACATAGATCCCTTC CAACCCATGAGTGGGCGGTTTAAGGACCGGGTGTCTTGGGATGGGAATCCTGAGCGGTACGA TGCCTCCATCCTTCTCTGGAAACTGCAGTTCGACGACAATGGGACATACACCTGCCAGGTGA AGAACCCACCTGATGTTGATGGGGTGATAGGGGGAGATCCGGCTCAGCGTCGTGCACACTGTA CGCTTCTCTGAGATCCACTTCCTGGCTCTGGCCATTGGCTCTGCCTGTGCACTGATGATCAT AATAGTAATTGTAGTGGTCCTCTTCCAGCATTACCGGAAAAAGCGATGGGCCGAAAGAGCTC ATAAAGTGGTGGAGATAAAATCAAAAGAAGAGGAAAGGCTCAACCAAGAGAAAAAAGGTCTCT GTTTATTTAGAAGACACAGACTAACAATTTTAGATGGAAGCTGAGATGATTTCCAAGAACAA GAACCCTAGTATTTCTTGAAGTTAATGGAAACTTTTCTTTGGCTTTTCCAGTTGTGACCCGT TTTCCAACCAGTTCTGCAGCATATTAGATTCTAGACAAGCAACACCCCTCTGGAGCCAGCAC AGTGCTCCTCCATATCACCAGTCATACACAGCCTCATTATTAAGGTCTTATTTAATTTCAGA GTGTAAATTTTTTCAAGTGCTCATTAGGTTTTATAAACAAGAAGCTACATTTTTGCCCTTAA GACACTACTTACAGTGTTATGACTTGTATACACATATATTGGTATCAAAGGGGATAAAAGCC AATTTGTCTGTTACATTTCCTTTCACGTATTTCTTTTAGCAGCACTTCTGCTACTAAAGTTA ATGTGTTTACTCTCTTTCCTTCCCACATTCTCAATTAAAAGGTGAGCTAAGCCTCCTCGGTG TTTCTGATTAACAGTAAATCCTAAATTCAAACTGTTAAATGACATTTTTATTTTTATGTCTC TTTGTCG

284/310

FIGURE 280

MYGKSSTRAVLLLLGIQLTALWPIAAVEIYTSRVLEAVNGTDARLKCTFSSFAPVGDALTVT WNFRPLDGGPEQFVFYYHIDPFQPMSGRFKDRVSWDGNPERYDASILLWKLQFDDNGTYTCQ VKNPPDVDGVIGEIRLSVVHTVRFSEIHFLALAIGSACALMIIIVIVVVLFQHYRKKRWAER AHKVVEIKSKEEERLNQEKKVSVYLEDTD

 ${\tt MKFLAVLVLLGVSIFLVSAQNPTTAAPADTYPATGPADDEAPDAETTAAATTATTAAPTTAT}$ ${\tt TAASTTARKDIPVLPKWVGDLPNGRVCP}$

GGACTCTGAAGGTCCCAAGCAGCTGCTGAGGCCCCCAAGGAAGTGGTTCCAACCTTGGACCC
CTAGGGGTCTGGATTTGCTGGTTAACAAGATAACCTGAGGGCAGGACCCCATAGGGGAA<u>ATG</u>C
TACCTCCTGCCCTTCCACCTGCCCTGGTGTTCACGGTGGCCTGGTCCCTCCTTGCCGAGAGA
GTGTCCTGGGTCAGGGACGCAGAGGACGCTCACAGACTCCAGCCCTTTGTTACCGAGAGAC
ACTTGGCAAGGTCCAGCGATGGTCCGGAGTCCACACACAGACTGGCGGCAGGGCAGGAGGGC
GACAGTTCTGTTGTGCTTGGTTGGACAGTAAGAGGGTCTTGGCCAGTCCAGGGTGGGGGCG
GCAAACTCCATAAAGAACCAGAGGGTCTGGGCCCCGGCCACAGAGTCATCTGCCCAGCTCCT
CTGCTGCTGGCCAGTGGGAGTGCACGAGGTGGGGCCGAGAAACCACAGGCTGG
ATTTGCCTGCGGGCCATGGTCCCTGTCTAGGGCAGCAATTCTCAACCTTCTTGCTCCAGGA
CCCCAAAGAGCTTTCATTGTATCTATTGATTTTTACCACATTAGCAATTAAAACCTAGGAAAAT
CACCTGAGATCAGGAGTTCAAGACCAGCCTGGCCAACATTGGGAGGCCGAGGCGGGTGGAT
CACCTGAGATCAGGAGTTCAAGACCAGCCTGGCCAACATTGGTGAAACCTTGTCTACTAAAAA
TACAAAAAATTAGCCAGGCACAGTGGTGCACTGGTAGTCCCAGTTACTCGGGAGGCTGAG
GCAGGAAAATCGCTTGAACCCAGGAGGCGGACGTTGCGGTGAGCCGAGATCGCGCCGCTGAT
TCCAGCCTGGCGACAAGAGTGAAACCTCATCTCACACA
TCCAGCCTGGCGACAAAGAGTGAGACTCCATCTCACACA

MLPPALPPALVFTVAWSLLAERVSWVRDAEDAHRLQPFVTERTLGKVQRWSGVHTQTGGRAG GGQFCCAWLDSKRVLASPGWGAANSIKNQRVWAPATESSAQLLCCWPVGVARGGALCQ

230/310

FIGURE 286

MPVPALCLLWALAMVTRPASAAPMGGPELAQHEELTLLFHGTLQLGQALNGVYRTTEGRLTK
ARNSLGLYGRTIELLGQEVSRGRDAAQELRASLLETQMEEDILQLQAEATAEVLGEVAQAQK
VLRDSVQRLEVQLRSAWLGPAYREFEVLKAHADKQSHILWALTGHVQRQRREMVAQQHRLRQ
IQERLHTAALPA

e91/310

FIGURE 287

GGCAACATGGCTCAGCAGGCTTGCCCCAGAGCCATGGCAAAGAATGGACTTGTAATTTGCAT CCTGGTGATCACCTTACTCCTGGACCAGACCACCAGCCACACATCCAGATTAAAAGCCAGGA **AGCACAGCAAACGTCGAGTGAGAGACAAGGATGGAGATCTGAAGACTCAAATTGAAAAGCTC** TAAAGTTCACAAGAAATGCTACCTTGCTTCAGAAGGTTTGAAGCATTTCCATGAGGCCAATG AAGACTGCATTTCCAAAGGAGGAATCCTGGTTATCCCCAGGAACTCCGACGAAATCAACGCC CTCCAAGACTATGGTAAAAGGAGCCTGCCAGGTGTCAATGACTTTTGGCTGGGCATCAATGA CATGGTCACGGAAGGCAAGTTTGTTGACGTCAACGGAATCGCTATCTCCTTCAACTGGG ACCGTGCACAGCCTAACGGTGGCAAGCGAGAAAACTGTGTCCTGTTCTCCCAATCAGCTCAG GGCAAGTGGAGTGATGAGGCCTGTCGCAGCAGCAAGAGATACATATGCGAGTTCACCATCCC TAAATAGGTCTTTCTCCAATGTGTCCTCCAAGCAAGATTCATCATAACTTATAGGTTCATGA TCTCTAAGATCAAGTAAAAATCATAATTTTTACTTATTAAAAAATTGCAACACAAGATCAAT GTCCATAGCAATATGATAGCATCAGCCAATTTTGCTAACACATTTCTTTGGGATTTTGCCCT TCCTGGGGTATAGGGGATCAGAAATATTGATCCATGTGCACGCAGATAAAATGGCTTCTGCT TTCCCTTGGAAGTTTAGCGTATGTTTGACTAACAAAAATTCCCTACATCAGAGACTCTAGGT GCTATATAATCCAAAAACTTTTCAGCCTGTTGCTCATTCTGTCCCATGCTGGCAATAATACC TTGTCAGCCCATTACCCTTATTTTGAATTGCTCCATCTCCTGGTGGGACTTGTATCTTGTCT TACCCTTTTTTTGGAAGTTTCCAGCCGCAATTTGAAATGAAATGACAAGGTGTATATTTGAT CAATTTTCATTCCCACCATTGCATTACAACCTCTAACTTAAATGGGTAACCCTAAGGCATAT AGCATCCTTACTCTCACCTTTTATGAGATTGAGAGTGGACTTACATTTCCTTTTTTACATTT TCGTATATTTATTTTTTTAGCCATCATTATATGTTTAAGTCTATTATGGGCAACCAATCTT TGGAAGCTGAAAACTGAATTTAAAGAATGCTATCTTGGAAAATTGCATACGTCTGTGCAATT TTTTATTCTGCCTAGTGCTATTCTGCTTGTTTAACTAGATTGTACAAAATAACTTCATTGCT TAATATCAAATTACAAAGTTTAGACTTGGAGGGAAATGGGCTTTTTAGAAGCAAACAATTTT AAATATATTTTGTTCTTCAAATAAATAGTGTTTAAACATTGAATGTGTTTTGTGAACAATAT CCCACTTTGCAAACTTTAACTACACATGCTTGGAATTAAGTTTTAGCTGTTTTCATTGCTCA

MAQQACPRAMAKNGLVICILVITLLLDQTTSHTSRLKARKHSKRRVRDKDGDLKTQIEKLWT EVNALKEIQALQTVCLRGTKVHKKCYLASEGLKHFHEANEDCISKGGILVIPRNSDEINALQ DYGKRSLPGVNDFWLGINDMVTEGKFVDVNGIAISFLNWDRAQPNGGKRENCVLFSQSAQGK WSDEACRSSKRYICEFTIPK

২ঙ্গ/১/১ FIGURE 289

セタイ/310 FIGURE 290

MKLAALLGLCVALSCSSAAAFLVGSAKPVAQPVAALESAAEAGAGTLANPLGTLNPLKLLLS SLGIPVNHLIEGSQKCVAELGPQAVGAVKALKALLGALTVFG

018/283-

FIGURE 291

TGAAGGACTTTTCCAGGACCCAAGGCCACACACTGGAAGTCTTGCAGCTGAAGGGAGGCACT CCTTGGCCTCCGCAGCCGATCACATGAAGGTGGTGCCAAGTCTCCTGCTCCTCCTG GCACAGGTGTGGCTGGTACCCGGCTTGGCCCCAGTCCTCAGTCGCCAGAGACCCCCAGCCCC TCAGAACCAGACCAGCAGGGTAGTGCAGGCTCCCAGGGAGGAAGAGAAGATGAGCAGGAGG CCAGCGAGGAGAAGGCCGGTGAGGAAGAGAAAGCCTGGCTGATGGCCAGCAGCAGCAGCTT GCCAAGGAGACTTCAAACTTCGGATTCAGCCTGCTGCGAAAGATCTCCATGAGGCACGATGG CAACATGGTCTTCTCTCCATTTGGCATGTCCTTGGCCATGACAGGCTTGATGCTGGGGGCCA CAGGGCCGACTGAAACCCAGATCAAGAGAGGGCTCCACTTGCAGGCCCTGAAGCCCACCAAG CCCGGGCTCCTGCCTTCTTTAAGGGACTCAGAGAGACCCTCTCCCGCAACCTGGAACT GGGCCTCTCACAGGGGAGTTTTGCCTTCATCCACAAGGATTTTGATGTCAAAGAGACTTTCT TCAATTTATCCAAGAGGTATTTTGATACAGAGTGCGTGCCTATGAATTTTCGCAATGCCTCA CAGGCCAAAAGGCTCATGAATCATTACATTAACAAAGAGACTCGGGGGAAAATTCCCAAACT GTTTGATGAGATTAATCCTGAAACCAAATTAATTCTTGTGGATTACATCTTGTTCAAAGGGA AATGGTTGACCCCATTTGACCCTGTCTTCACCGAAGTCGACACTTTCCACCTGGACAAGTAC AAGACCATTAAGGTGCCCATGATGTACGGTGCAGGCAAGTTTGCCTCCACCTTTGACAAGAA TTTTCGTTGTCATGTCCTCAAACTGCCCTACCAAGGAAATGCCACCATGCTGGTGGTCCTCA TGGAGAAAATGGGTGACCACCTCGCCCTTGAAGACTACCTGACCACAGACTTGGTGGAGACA GAAGTATGAGATGCATGAGCTGCTTAGGCAGATGGGAATCAGAAGAATCTTCTCACCCTTTG CTGACCTTAGTGAACTCTCAGCTACTGGAAGAAATCTCCAAGTATCCAGGGTTTTACGAAGA ACAGTGATTGAAGTTGAAAGGGGCACTGAGGCAGTGGCAGGAATCTTGTCAGAAATTAC TGCTTATTCCATGCCTCCTGTCATCAAAGTGGACCGGCCATTTCATTTCATGATCTATGAAG AAACCTCTGGAATGCTTCTGTTTCTGGGCAGGGTGGTGAATCCGACTCTCCTA<u>TAA</u>TTCAGG TACCAGCAATGGATGGCAGGGGAGAGTGTTCCTTTTGTTCTTAACTAGTTTAGGGTGTTCTC AAATAAATACAGTAGTCCCCACTTATCTGAGGGGGATACATTCAAAGACCCCCAGCAGATGC AAAGTTTAATTTATAAATTAGGCACAGTAAGAGATTAACAATAATAACAACATTAAGTAAAA TGAGTTACTTGAACGCAAGCACTGCAATACCATAACAGTCAAACTGATTATAGAGAAGGCTA CTAAGTGACTCATGGGCGAGGAGCATAGACAGTGTGGAGACATTGGGCAAGGGGAGAATTCA CATCCTGGGTGGGACAGAGCAGGACGATGCAAGATTCCATCCCACTACTCAGAATGGCATGC TGCTTAAGACTTTTAGATTGTTTATTTCTGGAATTTTTCATTTAATGTTTTTGGACCATGGT TGACCATGGTTAACTGAGACTGCAGAAAGCAAAACCATGGATAAGGGAGGACTACTACAAAA

MKVVPSLLLSVLLAQVWLVPGLAPSPQSPETPAPQNQTSRVVQAPREEEEDEQEASEEKAGE
EEKAWLMASRQQLAKETSNFGFSLLRKISMRHDGNMVFSPFGMSLAMTGLMLGATGPTETQI
KRGLHLQALKPTKPGLLPSLFKGLRETLSRNLELGLSQGSFAFIHKDFDVKETFFNLSKRYF
DTECVPMNFRNASQAKRLMNHYINKETRGKIPKLFDEINPETKLILVDYILFKGKWLTPFDP
VFTEVDTFHLDKYKTIKVPMMYGAGKFASTFDKNFRCHVLKLPYQGNATMLVVLMEKMGDHL
ALEDYLTTDLVETWLRNMKTRNMEVFFPKFKLDQKYEMHELLRQMGIRRIFSPFADLSELSA
TGRNLQVSRVLRRTVIEVDERGTEAVAGILSEITAYSMPPVIKVDRPFHFMIYEETSGMLLF
LGRVVNPTLL

২৭7/310 FIGURE 293

CTGGGATCAGCCACTGCAGCTCCCTGAGCACTCTCTACAGAGACGCGGACCCCAGACATGAG
GAGGCTCCTCCTGGTCACCAGCCTGGTGGTTGTGCTGCTGTGGGAGGCAGGTGCAGTCCCAG
CACCCAAGGTCCCTATCAAGATGCAAGTCAAACACTGGCCCTCAGAGCAGGACCCAGAGAAG
GCCTGGGGCGCCCGTGTGGTGGAGCCTCCGGAGAAGGACCAGCTGGTGGTGCTGTTCCC
TGTCCAGAAGCCGAAACTCTTGACCACCGAGGAGAAGCCACGAGGTCAGGGCAGGGCCCCA
TCCTTCCAGGCACCAAGGCCTGGATGGAGACCGAGGACACCCTGGGCCGTGTCCTGAGTCCC
GAGCCCGACCATGACAGCCTGTACCACCCTCCGCCTGAGGAGGACCAGGGCGAGGAGAGCC
CCGGTTGTGGGTGATGCCAAATCACCAGGTGCTCCTGGGACCGAGGAAGACCAAGACCACA
TCTACCACCCCCAGTAGGGCTCCAGGGGCCATCACTGCCCCCGCCTGTCCCAAGGCCCAGG
CTGTTGGGGACTGGGACCCTCCCTACCCTGCCCCAGCTAGACAAATAAACCCCCAGCAAGAACAAA

-≥38/>10 FIGURE 294

MRRLLLVTSLVVVLLWEAGAVPAPKVPIKMQVKHWPSEQDPEKAWGARVVEPPEKDDQLVVL FPVQKPKLLTTEEKPRGQGRGPILPGTKAWMETEDTLGRVLSPEPDHDSLYHPPPEEDQGEE RPRLWVMPNHQVLLGPEEDQDHIYHPQ

TACCCAAGGAAAGTGCAGCTGAGACTCAGACAAGATTACAATGAACCAACTCAGCTTCCTGC TGGACCTGTTCTTCGTCTCCATCTCTGCCCAGAAGCTGCAAGGAAATCAAAGACGAATGTCC TAGTGCATTTGATGGCCTGTATTTTCTCCGCACTGAGAATGGTGTTATCTACCAGACCTTCT GTGACATGACCTCTGGGGGTGGCGGCTGGACCCTGGTGGCCAGCGTGCATGAGAATGACATG CGTGGGAAGTGCACGGTGGGCGATCGCTGGTCCAGTCAGCAGGGCAGCAAAGCAGACTACCC AGAGGGGGACGCCAACTGCAACACCCTTTGGATCTGCAGAGGCGGCCACGAGCG ATGACTACAAGAACCCTGGCTACTACGACATCCAGGCCAAGGACCTGGGCATCTGGCACGTG CCCAATAAGTCCCCCATGCAGCACTGGAGAAACAGCTCCCTGCTGAGGTACCGCACGGACAC TGGCTTCCTCCAGACACTGGGACATAATCTGTTTGGCATCTACCAGAAATATCCAGTGAAAT ATGGAGAAGGAAAGTGTTGGACTGACAACGGCCCGGTGATCCCTGTGGTCTATGATTTTGGC GACGCCAGAAAACAGCATCTTATTACTCACCCTATGGCCAGCGGGAATTCACTGCGGGATT TGTTCAGTTCAGGGTATTTAATAACGAGAGAGCCGCCAACGCCTTGTGTGCTGGAATGAGGG TCACCGGATGTAACACTGAGCATCACTGCATTGGTGGAGGAGGATACTTTCCAGAGGCCAGT CCCCAGCAGTGTGGAGATTTTTCTGGTTTTGATTGGAGTGGATATGGAACTCATGTTGGTTA CAGCAGCAGCCGTGAGATAACTGAGGCAGCTGTGCTTCTATTCTATCGTTGAGAGTTTTGTG GGAGGGAACCCAGACCTCTCCCCAACCATGAGATCCCAAGGATGGAGAACAACTTACCCA GTAGCTAGAATGTTAATGGCAGAAGAGAAAACAATAAATCATATTGACTCAAGAAAAAAA

MNQLSFLLFLIATTRGWSTDEANTYFKEWTCSSSPSLPRSCKEIKDECPSAFDGLYFLRTEN GVIYQTFCDMTSGGGGWTLVASVHENDMRGKCTVGDRWSSQQGSKADYPEGDGNWANYNTFG SAEAATSDDYKNPGYYDIQAKDLGIWHVPNKSPMQHWRNSSLLRYRTDTGFLQTLGHNLFGI YQKYPVKYGEGKCWTDNGPVIPVVYDFGDAQKTASYYSPYGQREFTAGFVQFRVFNNERAAN ALCAGMRVTGCNTEHHCIGGGGYFPEASPQQCGDFSGFDWSGYGTHVGYSSSREITEAAVLLFYR

301/310

FIGURE 297

GCGGAGCCGGCGCCGCCAGAGGAGCCGCTCTCGCCGCCGCCACCTCGGCTGGGAGCC ${\tt CACGAGGCTGCCGCATCCTGCCCTCGGAACA} \underline{{\tt ATG}} {\tt GGACTCGGCGCGAGGTGCTTGGGCCG}$ CGCTGCTCCTGGGGACGCTGCAGGTGCTAGCGCTGCTGGGGGCCCCCATGAAAGCGCAGCC ATGGCGGCATCTGCAAACATAGAGAATTCTGGGCTTCCACACAACTCCAGTGCTAACTCAAC AGAGACTCTCCAACATGTGCCTTCTGACCATACAAATGAAACTTCCAACAGTACTGTGAAAC CACCAACTTCAGTTGCCTCAGACTCCAGTAATACAACGGTCACCACCATGAAACCTACAGCG GCATCTAATACAACAACACCAGGGATGGTCTCAACAAATATGACTTCTACCACCTTAAAGTC TACACCCAAAACAACAAGTGTTTCACAGAACACATCTCAGATATCAACATCCACAATGACCG TAACCCACAATAGTTCAGTGACATCTGCTGCTTCATCAGTAACAATCACAACAACTATGCAT TCTGAAGCAAAGAAAGGATCAAAATTTGATACTGGGAGCTTTGTTGGTGGTATTGTATTAAC GCTGGGAGTTTTATCTATTCTTTACATTGGATGCAAAATGTATTACTCAAGAAGAGGCATTC GGTATCGAACCATAGATGAACATGATGCCATCATT<u>TAA</u>GGAAATCCATGGACCAAGGATGGA ATACAGATTGATGCTGCCCTATCAATTAATTTTGGTTTATTAATAGTTTAAAACAATATTCT CTTTTTGAAAATAGTATAAACAGGCCATGCATATAATGTACAGTGTATTACGTAAATATGTA AAGATTCTTCAAGGTAACAAGGGTTTGGGTTTTGAAATAAACATCTGGATCTTATAGACCGT GGGGTGGGGGCATTGGTCACATATGACCAGTAATTGAAAGACGTCATCACTGAAAGACAGAA TGCCATCTGGGCATACAAATAAGAAGTTTGTCACAGCACTCAGGATTTTGGGTATCTTTTGT AGCTCACATAAAGAACTTCAGTGCTTTTCAGAGCTGGATATATCTTAATTACTAATGCCACA CAGAAATTATACAATCAAACTAGATCTGAAGCATAATTTAAGAAAAACATCAACATTTTTTG TGCTTTAAACTGTAGTAGTTGGTCTAGAAACAAAATACTCC

∞2/310 FIGURE 298

MGLGARGAWAALLLGTLQVLALLGAAHESAAMAASANIENSGLPHNSSANSTETLQHVPSDH TNETSNSTVKPPTSVASDSSNTTVTTMKPTAASNTTTPGMVSTNMTSTTLKSTPKTTSVSQN TSQISTSTMTVTHNSSVTSAASSVTITTTMHSEAKKGSKFDTGSFVGGIVLTLGVLSILYIG CKMYYSRRGIRYRTIDEHDAII

303/310

FIGURE 299

CAGCCGGGTCCCAAGCCTGTGCCTGAGCCTGAGCCTGAGCCTGAGCCCGAGCCGGGAGCCGG TCGCGGGGGCTCCGGGCTGTGGGACCGCTGGGGCCCCCAGCG<u>ATG</u>GCGACCCTGTGGGGAGGC CTTCTTCGGCTTGGCTCCTCAGCCTGTCGTGCCTGGCGCTTTCCGTGCTGCTGCTGGC ATAAAGAAAATTCTGGGCATATTTATAATAAGAACATATCTCAGAAAGATTGTGATTGCCTT CATGTTGTGGAGCCCATGCCTGTGCGGGGGCCTGATGTAGAAGCATACTGTCTACGCTGTGA ATGCAAATATGAAGAAAGAAGCTCTGTCACAATCAAGGTTACCATTATAATTTATCTCTCCA TTTTGGGCCTTCTACTTCTGTACATGGTATATCTTACTCTGGTTGAGCCCATACTGAAGAGG CGCCTCTTTGGACATGCACAGTTGATACAGAGTGATGATGATATTGGGGATCACCAGCCTTT TGCAAATGCACACGATGTGCTAGCCCGCTCCCGCAGTCGAGCCAACGTGCTGAACAAGGTAG CATGTTGTCCTCAGC<u>TAA</u>TTGGGAATTGAATTCAAGGTGACTAGAAAGAAACAGGCAGACAA CTGGAAAGAACTGACTGGGTTTTGCTGGGTTTCATTTTAATACCTTGTTGATTTCACCAACT ATAATAGAGACATTTTTAAAAGCACACAGCTCAAAGTCAGCCAATAAGTCTTTTCCTATTTG TGACTTTTACTAATAAAATAAATCTGCCTGTAAATTATCTTGAAGTCCTTTACCTGGAACA AGCACTCTCTTTTTCACCACATAGTTTTAACTTGACTTTCAAGATAATTTTCAGGGTTTTTG TTGTTGTTGTTTTTGTTTGTTTTGGTGGGAGAGGGGAGGGATGCCTGGGAAGTGGTT **AACAACTTTTTTCAAGTCACTTTACTAAACAAACTTTTGTAAATAGACCTTACCTTCTATTT** TCGAGTTTCATTTATATTTTGCAGTGTAGCCAGCCTCATCAAAGAGCTGACTTACTCATTTG ACTTTTGCACTGACTGTATTATCTGGGTATCTGCTGTGTCTGCACTTCATGGTAAACGGGAT CTAAAATGCCTGGTGGCTTTTCACAAAAAGCAGATTTTCTTCATGTACTGTGATGTCTGATG CAATGCATCCTAGAACAAACTGGCCATTTGCTAGTTTACTCTAAAGACTAAACATAGTCTTG GTGTGTGTGTGTCTTACTCATCTTCTAGTACCTTTAAGGACAAATCCTAAGGACTTGGACACT TGCAATAAAGAAATTTTATTTTAAACCCAAGCCTCCCTGGATTGATAATATATACACATTTG TCAGCATTTCCGGTCGTGGTGAGAGGCAGCTGTTTGAGCTCCAATATGTGCAGCTTTGAACT AGGGCTGGGGTTGTGGGTGCCTCTTCTGAAAGGTCTAACCATTATTGGATAACTGGCTTTTT TCTTCCTATGTCCTCTTTGGAATGTAACAATAAAAATAATTTTTGAAACATCAA

MATLWGGLLRLGSLLSLSCLALSVLLLAQLSDAAKNFEDVRCKCICPPYKENSGHIYNKNIS
QKDCDCLHVVEPMPVRGPDVEAYCLRCECKYEERSSVTIKVTIIIYLSILGLLLLYMVYLTL
VEPILKRRLFGHAQLIQSDDDIGDHQPFANAHDVLARSRSRANVLNKVEYAQQRWKLQVQEQ
RKSVFDRHVVLS

WO 99/63088

305/310 FIGURE 301

MAYSTVQRVALASGLVLALSLLLPKAFLSRGKRQEPPPTPEGKLGRFPPMMHHHQAPSDGQT PGARFQRSHLAEAFAKAKGSGGGAGGGGGGGGGGGGGGIMGQIIPIYGFGIFLYILYILFKVSRIILI ILHQ

CGGCTCGAGTGCAGCTGTGGGGAGATTTCAGTGCATTGCCTCCCCTGGGTGCTCTTCATCTT GGATTTGAAAGTTGAGAGCAGC<u>ATG</u>TTTTGCCCACTGAAACTCATCCTGCTGCCAGTGTTAC TGGATTATTCCTTGGGCCTGAATGACTTGAATGTTTCCCCGCCTGAGCTAACAGTCCATGTG GGTGATTCAGCTCTGATGGGATGTTTTTCCAGAGCACAGAAGACAAATGTATATTCAAGAT AGACTGGACTCTGTCACCAGGAGAGCACGCCAAGGACGAATATGTGCTATACTATTACTCCA ATCTCAGTGTGCCTATTGGGCGCTTCCAGAACCGCGTACACTTGATGGGGGACATCTTATGC **AATGATGGCTCTCTCCTGCTCCAAGATGTGCAAGAGGCTGACCAGGGAACCTATATCTGTGA** AATCCGCCTCAAAGGGGAGAGCCAGGTGTTCAAGAAGGCGGTGGTACTGCATGTGCTTCCAG AGCACAGAAGTGAAACACGTGACCAAGGTAGAATGGATATTTTCAGGACGCGCGCAAAGGA GGAGATTGTATTTCGTTACTACCACAAACTCAGGATGTCTGTGGAGTACTCCCAGAGCTGGG GCCACTTCCAGAATCGTGTGAACCTGGTGGGGGACATTTTCCGCAATGACGGTTCCATCATG CTTCAAGGAGTGAGGGAGTCAGATGGAGGAAACTACACCTGCAGTATCCACCTAGGGAACCT GGTGTTCAAGAAAACCATTGTGCTGCATGTCAGCCCGGAAGAGCCCTCGAACACTGGTGACCC CGGCAGCCCTGAGGCCTCTGGTCTTGGGTGATCAGTTGGTGATCATTGTGGGAATTGTC TGTGCCACAATCCTGCTGCTCCCTGTTCTGATATTGATCGTGAAGAAGACCTGTGGAAATAA GAGTTCAGTGAATTCTACAGTCTTGGTGAAGAACACGAAGAAGACTAATCCAGAGATAAAAG AAAAACCCTGCCATTTTGAAAGATGTGAAGGGGAGAAACACATTTACTCCCCAATAATTGTA CGGGAGGTGATCGAGGAAGAAGAACCAAGTGAAAAATCAGAGGCCACCTACATGACCATGCA CCCAGTTTGGCCTTCTCTGAGGTCAGATCGGAACAACTCACTTGAAAAAAAGTCAGGTGGGG GAATGCCAAAAACACAGCAAGCCTTT<u>TGA</u>GAAGAATGGAGAGTCCCTTCATCTCAGCAGCGG TGGAGACTCTCTCTGTGTGTGTCCTGGGCCACTCTACCAGTGATTTCAGACTCCCGCTCTC CCAGCTGTCCTCGTCTCATTGTTTGGTCAATACACTGAAGATGGAGAATTTGGAGCCTGG CTCTGGAGTGGGACACTGGCCCTGGGAACCAGGCTGAGCTGAGTGGCCTCAAACCCCCCGTT GGATCAGACCCTCCTGTGGGCAGGGTTCTTAGTGGATGAGTTACTGGGAAGAATCAGAGATA AAAACCAACCCAAATCAA

MFCPLKLILLPVLLDYSLGLNDLNVSPPELTVHVGDSALMGCVFQSTEDKCIFKIDWTLSPG
EHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDILCNDGSLLLQDVQEADQGTYICEIRLKGES
QVFKKAVVLHVLPEEPKELMVHVGGLIQMGCVFQSTEVKHVTKVEWIFSGRRAKEEIVFRYY
HKLRMSVEYSQSWGHFQNRVNLVGDIFRNDGSIMLQGVRESDGGNYTCSIHLGNLVFKKTIV
LHVSPEEPRTLVTPAALRPLVLGGNQLVIIVGIVCATILLLPVLILIVKKTCGNKSSVNSTV
LVKNTKKTNPEIKEKPCHFERCEGEKHIYSPIIVREVIEEEEPSEKSEATYMTMHPVWPSLR
SDRNNSLEKKSGGGMPKTQQAF

FIGURE 305

CTATGAAGAAGCTTCCTGGAAAACAATAAGCAAAGGAAAACAAATGTGTCCCCATCTCACATG GTTCTACCCTACTAAAGACAGGAAGATCATAAACTGACAGATACTGAAAATTGTAAGAGTTGG ${\tt AAACTACATTTTGCAAAGTCATTGAACTCTGAGCTCAGTTGCAGTACTCGGGAAGCC} {\tt ATGCA}$ GGATGAAGATGGATACATCACCTTAAATATTAAAAACTCGGAAACCAGCTCTCGTCTCCGTTG GCCCTGCATCCTCCTGGTGGCGTGTGATGGCTTTGATTCTGCTGATCCTGTGCGTGGGG ATGGTTGTCGGGCTGGTGGCTCTGGGGATTTGGTCTGTCATGCAGCGCAATTACCTACAAGA TGAGAATGAAAATCGCACAGGAACTCTGCAACAATTAGCAAAGCGCTTCTGTCAATATGTGG TAAAACAATCAGAACTAAAGGGCACTTTCAAAGGTCATAAATGCAGCCCCTGTGACACAAAC TGGAGATATTATGGAGATAGCTGCTATGGGTTCTTCAGGCACAACTTAACATGGGAAGAGAG TAAGCAGTACTGCACTGACATGAATGCTACTCTCCTGAAGATTGACAACCGGAACATTGTGG AGTACATCAAAGCCAGGACTCATTTAATTCGTTGGGTCGGATTATCTCGCCAGAAGTCGAAT GAGGTCTGGAAGTGGGAGGATGGCTCGGTTATCTCAGAAAATATGTTTGAGTTTTTGGAAGA TGGAAAAGGAAATATGAATTGTGCTTATTTTCATAATGGGAAAATGCACCCTACCTTCTGTG AGAACAAACATTATTTAATGTGTGAGAGGAAGGCTGGCATGACCAAGGTGGACCAACTACCT **TAA**TGCAAAGAGGTGGACAGGATAACACAGATAAGGGCTTTATTGTACAATAAAAGATATGT ATGAATGCATCAGTAGCTGAAAAAAAAAAAAAA

MQDEDGYITLNIKTRKPALVSVGPASSSWWRVMALILLILCVGMVVGLVALGIWSVMQRNYL QDENENRTGTLQQLAKRFCQYVVKQSELKGTFKGHKCSPCDTNWRYYGDSCYGFFRHNLTWE ESKQYCTDMNATLLKIDNRNIVEYIKARTHLIRWVGLSRQKSNEVWKWEDGSVISENMFEFL EDGKGNMNCAYFHNGKMHPTFCENKHYLMCERKAGMTKVDQLP

PCT/US99/12252

(30) 60/088,742	10 Jun/juin 19 98 (10.06.1998)	US	(30) 60/090,254	22 Jun/juin 1998 (22.06.1998)	US	(30) 60/091,478	2 Jul/juli 1998 (02.07.1998)	US
(30) 60/088,810	10 Jun/juin 1998 (10.06.1998)	US	(30) 60/090,355	23 Jun/juin 1998 (23.06.1998)	US	(30) 60/091,626	2 Jul/juil 1998 (02.07.1998)	US
(30) 60/088,811	10 Jun/juin 1998 (10.06.1998)	US	(30) 60/090,349	23 Jun/juin 1998 (23,06,1998)	US	(30) 60/091,628	2 Jul/juil 1998 (02.07.1998)	US
(30) 60/088,824	10 Jun/juin 1998 (10.06.1998)	US	(30) 60/090,429	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/091,633	2 Jul/juli 1998 (02.07.1998)	US
(30) 60/088,825	10 Jun/juin 1998 (10.06.1998)	us	(30) 60/090,431	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/091,646	2 Jul/juli 1998 (02.07.1998)	US
(30) 60/088,826	10 Jun/juin 1998 (10.06.1998)	US	(30) 60/090,435	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/091,673	2 Jul/juil 1998 (02.07.1998)	US
(30) 60/088,858	11 Jun/j uin 1998 (11.06.19 98)	US ·	(30) 60/090,444	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/091,978	7 Ju l/juil 1998 (07.07.1998)	US
(30) 60/088,861	11 Jun/juin 1998 (11.06.1998)	US	(30) 60/090,445	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/091,982	7 Jul/juil 1998 (07.07.1998)	US
(30) 60/088,863	11 Jun/juin 1998 (11.06.1998)	US	(30) 60/090,461	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/092,182	9 Jul/jull 1998 (09.07.1998)	US
(30) 60/088,876	11 Jun/juin 1998 (11.06.1998)	US	(30) 60/090,472	24 Jun/juin 19 9 8 (24.06.1998)	US	(30) 60/092,472	10 Jul/juil 1998 (10.07.1998)	US
(30) 60/089,090	12 Jun/juin 1998 (12.06.1998)	US	(30) 60/090,535	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/093,339	20 Jul/juil 1998 (20.07.1998)	us
(30) 60/089,105	12 Jun/juin 1998 (12.06.1998)	บร	(30) 60/090,538	24 Jun/juin 1998 (24.06.19 98)	US	(30) 60/094,651	30 Jul/juil 1998 (30.07.1998)	us
(30) 60/089,440	16 Jun/juin 1998 (16.06.1998)	US	(30) 60/090,540	24 Jun/juin 1998 (24.06.1996)	US	(30) 60/095,282	4 Aug/août 1998 (04.08.1998)	US
(30) 60/089,512	16 Jun/juin 1998 (16.06.1998)	US	(30) 60/090,557	24 Jun/juin 1998 (24.06.1998)	US	(30) 60/095,285	4 Aug/août 1998 (04.08.1998) 4 Aug/août 1998	US
(30) 60/089,514	16 Jun/juin 1998 (16.06.1998)	US	(30) 60/090,676	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/095,301	(04.08.1998) 4 Aug/août 1998	US
(30)·60/089,532	17. Jun/juin 1998.	US_	(30) 60/090,678	25. Jun/juln .1998.	us_	(30) 60/093,302	(04.08.1998)	
(50) 00000,000	(17.06.1998)		(30, 30, 31, 31, 31, 31, 31, 31, 31, 31, 31, 31	(25.06.1998)		(30) 60/095,318	4 Aug/août 1998	US
(30) 60/089,538	17 Jun/juin 1998 (17,06.1998)		(30) 60/090,688	25 Jun/juin 1998 (25.06.1998)	US	(30) 60/095,321	(04.08.1998) 4 Ang/août 1998	us
(30) 60/089,598	17 Jun/juin 1998 (17.06.1998)		(30) 60/090,690	25 Jun/juin 1998 (25.06.19 9 8)	US	(30) 60/095,325	(04.08.1998) 4 Aug/août 1998 (04.08.1998)	us
(30) 60/089,599	17 Jun/juin 1998 (17.06.1998)	US	(30) 60/090,691	25 Jun/Juin 1998 (25.06.1998)	US	max comme 016	10 Aug/act 1998	us
(30) 60/089,600	17 Jun/juin 1998	US	(30) 60/090,694	25 Jun/juln 1998	US	(30) 60/095,916	(10.08.1998)	
(30) 60/089,653	(17.06.1998) 17 Jun/juin 1998	s US	(30) 60/090,695	(25.06.1998) 25 Jun/juin 1998	US	(30) 60/095,929	10 Aug/août 1998 (10.08.1998)	US
	(17.06.1998)			(25.06.1998)		(30) 60/096,012	10 Aug/2001 1998 (10.08.1998)	US
(30) 60/089,801	18 Jun/juin 1998 (18.06.1998)		(30) 60/090,696	25 Jun/juin 1998 (25.06.1998)		(30) 60/096,143	11 Aug/août 1998 (11.08.1998)	US
(30) 60/089,907	18 Jun/juin 1990 (18.06.1998)		(30) 60/090,862	26 Jun/juin 1998 (26.06.1998)		(30) 60/096,146	11 Aug/août 1995 (11.08.1998)	US
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(43) International Publication Date 9 December 1999 (09.12.1999)

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(20)	Priority Data:	•		60/089,948	19 June 1998 (19.06.1998)	US
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(54) Title: MEMBRANE-BOUND PROTEINS AND NUCLEIC ACIDS ENCODING THE SAME

(57) Abstract: The present invention is directed to membrane-bound polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

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- (74) Agents: KRESNAK, Mark, T. et al.; Genentech, Inc., 1 DNA Way, South San Francisco, CA 94080-4990 (US).
- (81) Designated States (national): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

- With international search report.
- (88) Date of publication of the international search report: 29 March 2001
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 Previous Correction:
 see PCT Gazette No. 42/2000 of 19 October 2000, Section II

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

International Application No PCT/US 99/12252

According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 6 C12N C07 K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched. Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Category* CRation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 6 C12N C07K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched. Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT	Relevant to claim No.
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considered to be or particular relevance; the citemational "X" document of particular relevance; the citemational	imed invention
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"C" document which may throw doubts an priority desired." "Y" document of particular relevance; the dis	umed invention
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other means other means in the art. "P" document published prior to the international filing date but "&" document member of the same patent to	
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PCT/US 99/12252

Box I C	bservations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Intern	national Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. 🔲 🖁	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2 X	Claims Nos.: 1,5-11 all incompl. Claims Nos.: 1,5-11 all incompl. because they relate to parts of the international Application that do not comply with the prescribed requirements to such
	because they relate to parts of the international Apparatus and the carried out, specifically an extent that no meaningful International Search can be carried out, specifically see FURTHER INFORMATION sheet PCT/ISA/210
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box ii	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inte	emational Searching Authority found multiple inventions in this international application, as follows:
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
	n. n.t. t. t
4. [2	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: invention 1. claims 1-26 (all partially)
Po-m	The additional search fees were accompanied by the applicant's protest
Hem	No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1,5-11 (all incompletely)

Claims 1 and 5-11 relate to polynucleotides defined as having at least 80% sequence identity to a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence selected from a group of polypeptides listed in claim 1 (SEQ.IDs. 2, 6, 8, 14, 20). Back-translation of the polypeptide into DNA generates a very great number of nucleic acid sequences. It is not possible to search an entire database with this enormous set of sequences. The search thus has been limited to nucleic acid sequences having at least 80% homology with the nucleotide sequences as listed in claim 2 (SEQ.IDs. 1, 5, 7, 13, 19).

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Claims: Invention 1: Claims 1-26 (all partially)

A membrane-bound protein as represented by SEQ.ID.2 and variants having 80% amino acid sequence identity therewith, a nucleic acid encoding said protein as represented by SEQ.ID.1 and variants having 80% nucleotide sequence identity therewith; a vector comprising said nucleic acid; a host cell comprising said vector; a process for the production of said protein; a chimeric molecule comprising said protein; an antibody specific for said protein; an extracellular domain of said protein; and a variant of said protein lacking its signal sequence.

2. Claims: Inventions 2-135: Claims 1-26 (all partially)

Idem as subject 1 but limited to one DNA sequence selected from SEQ.IDs. 1-424 and the corresponding polypeptide, wherein invention 2 is limited to SEQ.IDs. 5 and 6, invention 3 is limited to SEQ.IDs. 7 and 8, invention 4 is limited to SEQ.IDs. 13 and 14 and invention 135 is limited to SEQ.IDs. 423 and 424.

Information on patent family members

International Application No PCT/US 99/12252

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